Liver Transplantation in the Era of Artificial Intelligence: Surgical Innovation, Risk Stratification, and Patient-centred Care

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Received May 19, 2025; Accepted June 2, 2026.

Key words: Artificial intelligence – Liver transplantation – Risk stratification – Graft viability – Transplant outcomes

Abstract: Liver transplantation continues to be the most effective and, in many cases, the only therapeutic recourse for individuals suffering from end-stage liver disease, select hepatocellular malignancies, and uncommon hepatic disorders. Alongside clinical advancements, artificial intelligence (AI) is increasingly being explored for its capacity to support clinical decision-making at all stages of the transplant continuum. In this narrative review, we synthesize recent advancements in liver transplantation and examine the expanding role of AI throughout the process. AI-driven technologies have demonstrated the ability to improve donor-recipient compatibility, evaluate graft function, interpret diagnostic images, and support post-surgical monitoring. Still, obstacles such as limited data availability, bias within algorithms, and unresolved ethical questions continue to pose challenges. At the same time, innovations like machine perfusion, synthetic grafts, and predictive models are helping refine surgical procedures and post-transplant care. Introducing AI into the transplant workflow may boost accuracy, fairness, and healthcare quality. A patient-centred approach that incorporates modern technology, mental health resources, and ethical responsibility will be essential for the future of liver transplantation.

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https://doi.org/10.14712/23362936.2026.11

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Introduction

Liver transplantation (LT) remains a well-established and life-saving intervention for individuals with end-stage liver disease (ESLD), hepatocellular carcinoma (HCC), and acute liver failure (ALF). Over the past 20 years, changes in the global distribution of liver disease have influenced transplant eligibility criteria. In Western countries, nonalcoholic fatty liver disease (NAFLD) has become the leading cause of LT, whereas viral hepatitis continues to be the primary indication in parts of Asia, Africa, and South America (Cichoż-Lach et al., 2012; Safi et al., 2025). These epidemiological patterns highlight the need for region-specific transplant strategies tailored to local liver disease profiles.

Although significant progress has been made in surgical procedures and immunosuppressive treatments, several persistent challenges remain. These include a chronic shortage of donor organs, variability in patient outcomes after transplantation, and increasing complexity in selecting appropriate candidates. Moreover, non-medical factors such as frailty, psychological stress, and regret from living donors further complicate outcomes and are often insufficiently addressed in existing care models (Accardo et al., 2023; Hill et al., 2023).

At the same time, introducing artificial intelligence (AI) into clinical medicine creates new avenues for improving transplant success. AI tools, including machine learning algorithms, deep learning networks, and imaging-based platforms, have shown promise in enhancing diagnostic precision, improving donor-recipient compatibility, and monitoring patients postoperatively. These technologies can support decision-making, especially when traditional methods fall short (Balsano et al., 2023; Singhal et al., 2024; Zhang et al., 2024). Nevertheless, challenges such as limited data diversity, lack of algorithm transparency, and underdeveloped regulatory frameworks continue to hinder widespread implementation.

This review offers an in-depth overview of recent developments in liver transplantation, explicitly focusing on integrating AI into surgical and clinical practice. It explores updated transplant indications, advancements in surgical innovation, infection control strategies, and outcome monitoring. Furthermore, it examines ethical implications, translational hurdles, and future directions for research and practice in settings with varying healthcare resources.

From candidate selection to risk stratification: Foundations for AI-enhanced allocation

Patient selection for LT has evolved substantially in response to shifting disease burdens, expanded indications, and improved understanding of prognostic determinants (Battistella et al., 2024). Historically dominated by viral hepatitis and alcohol-related liver disease, the global LT landscape now reflects the increasing prevalence of NAFLD in Western populations. In contrast, hepatitis B and C

Table 1: Risk stratification models

Model name (Ref.)	Variables considered	Application phase	Predictive strength	Limitations
MELD (Chung et al., 2023)	Bilirubin, INR, creatinine	Pre	Good for short-term mortality	Does not account for functional status
MELD-Na (Chung et al., 2023)	Bilirubin, INR, creatinine, sodium	Pre	Improved over MELD; better for hyponatremia cases	Limited granularity in frail patients
APACHE IV (Hu et al., 2013; Hamilton et al., 2021; Matsushima et al., 2025)	Physiologic parameters, chronic health data	Post	High predictive accuracy in ICU settings	Complexity and data requirements
GEMA-AI (Gómez-Orellana et al., 2025)	Sociodemographics, clinical data	Pre	Superior to MELD-Na and MELD 3.0 for waitlist outcomes	Requires AI infrastructure and validation
Optimal Classification Trees (OCT) (Briceño et al., 2020)	Clinical, demographic, and functional data	Pre	Interpretable and customizable prediction models	Dependent on data quality and interpretability
Frailty tools (e.g., KPS) (Balogh et al., 2025)	Physical function, performance status	Pre and post	Predictive of long-term survival, especially post-transplant	KPS lacks granularity; validation needed for other tools

MELD – Model for End-Stage Liver Disease; MELD-Na – Model for End-Stage Liver Disease with sodium; APACHE IV – Acute Physiology and Chronic Health Evaluation IV; GEMA-AI – Generalizable Model for Early Allograft Dysfunction using Artificial Intelligence; KPS – Karnofsky Performance Status; AI – artificial intelligence; ICU – intensive care unit

predominate in Asia, Africa, and Latin America (Cichoż-Lach et al., 2012; Safi et al., 2025). These patterns necessitate region-specific approaches to transplant eligibility and health system planning.

Emerging data support the inclusion of patients with severe alcohol-associated hepatitis (AAH) under early transplant protocols, provided that stringent selection criteria are applied. Studies demonstrate that, despite increased infection risk, early LT in well-screened AAH patients yields favourable outcomes (Kulkarni et al., 2023). Similarly, rare indications such as metabolic liver disease and intrahepatic cholangiocarcinoma (iCCA) are increasingly considered in highly selected cases, often guided by neoadjuvant protocols or multidisciplinary consensus (Panayotova et al., 2021).

Risk stratification is central to transplantation decisions, influencing prioritisation of waitlist and post-transplant outcomes. The Model for End-Stage Liver Disease (MELD) score and its sodium-adjusted variant MELD-Na are widely used to estimate short-term mortality risk and allocate deceased donor organs (Chung et al., 2023). However, evidence suggests dynamic scoring systems such as the Acute Physiology and Chronic Health Evaluation (APACHE IV) may offer superior predictive validity in orthotopic liver transplant intensive care settings (Hu et al., 2013; Hamilton et al., 2021; Matsushima et al., 2025). In particular, APACHE IV has shown enhanced accuracy in identifying candidates at risk for early postoperative mortality, with patients scoring within a MELD range of 15–25 exhibiting the lowest observed mortality in some cohorts (Hamilton et al., 2021).

Frailty has emerged as a critical, modifiable determinant of both pre-and post-transplant outcomes. Unlike biochemical indices, frailty reflects physiologic reserve and functional status, often providing greater prognostic utility in long-term survival than MELD alone (Balogh et al., 2025). The Karnofsky Performance Status (KPS), while widely used by the Organ Procurement and Transplantation Network (OPTN), remains a coarse surrogate, and efforts are ongoing to validate more granular tools tailored to LT populations.

Socioeconomic and geographic disparities also influence access to transplantation. Regional variation in organ procurement efficiency, insurance status, and healthcare infrastructure contributes to differences in MELD scores at listing, waitlist attrition, and time to transplant (Lentine et al., 2023; Yilma et al., 2023). These inequities emphasise the need for equity-informed allocation frameworks and risk models that incorporate social determinants of health. These evolving criteria reflect a broader shift toward individualised, multidimensional assessment of transplant candidates. As predictive analytics and AI-driven tools mature, they may further refine risk stratification by integrating clinical, functional, and sociodemographic data to guide patient selection (Table 1).

Artificial intelligence in liver transplantation

AI is emerging as a transformative force in liver transplantation, offering advanced analytical capabilities beyond traditional clinical judgment (Figure 1). AI applications enhance diagnostic accuracy, optimise organ allocation, and enable dynamic monitoring across the transplant continuum by integrating high-dimensional data from imaging, clinical records, and laboratory parameters. Although still in the early stages of clinical integration, these tools can augment decision-making and improve outcomes, particularly when implemented within structured, multidisciplinary frameworks.

Diagnostic enhancement

AI-enabled diagnostic platforms have demonstrated significant promise in detecting and characterising hepatocellular carcinoma (HCC). Machine learning

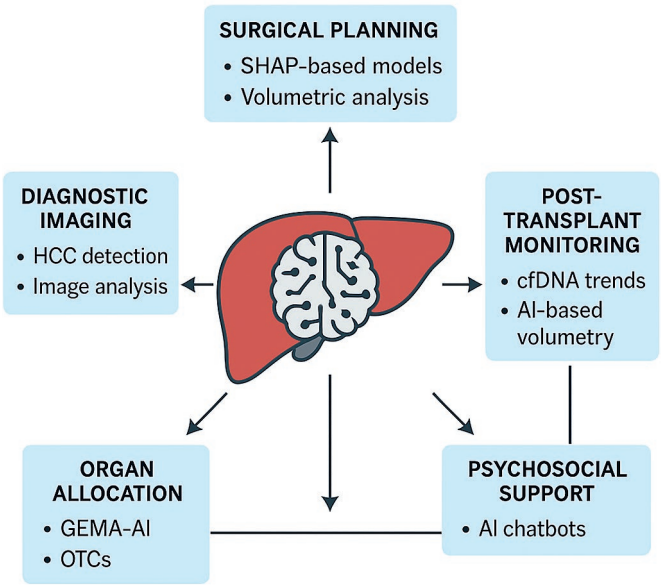

Figure 1: Framework of artificial intelligence (AI) applications across the liver transplantation. This figure presents a conceptual framework illustrating how AI is applied throughout the liver transplantation continuum. It highlights five key domains – diagnostic imaging, surgical planning, organ allocation, post-transplant monitoring, and psychosocial support – each supported by specific AI tools. These include machine learning for hepatocellular carcinoma (HCC) detection, SHapley Additive exPlanations (SHAP)-based surgical risk models, AI-enhanced volumetric analysis, predictive analytics for graft monitoring, and chatbot-assisted mental health support.

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algorithms applied to ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) have shown high sensitivity in identifying hepatic lesions and differentiating malignancies (Nishida and Kudo, 2022; Pomohaci et al., 2023). These tools can support earlier diagnosis, potentially expanding access to transplantation among patients with limited-stage HCC. Furthermore, radiomics and non-invasive image-based biomarkers may reduce dependence on histologic confirmation, minimising biopsy-associated risks (Malik et al., 2024).

Innovations such as LiverColor, a smartphone-integrated AI application, exemplify the growing accessibility of diagnostic technologies. Designed for use in low-resource settings, LiverColor leverages mobile camera input and machine learning models to estimate liver fat content, providing a scalable, cost-effective screening solution (Zsombor et al., 2023; Gómez-Gavara et al., 2024).

Surgical planning and organ allocation

In surgical planning, AI has been utilized to predict operative complexity and resource requirements. For example, explainable AI models using SHAP (SHapley Additive exPlanations) have been employed to assess the likelihood of conversion from laparoscopic to open surgery in segment 7 and 8 resections, offering real-time surgical risk profiling (Lopez-Lopez et al., 2024). AI-assisted tools also facilitate preoperative volumetric assessments to predict safe resection margins and reduce the incidence of post-hepatectomy liver failure (Kang et al., 2024).

Machine learning models are increasingly employed in organ allocation to supplement or refine existing scoring systems. The Gender-Equity Model for Allocation using Artificial Intelligence (GEMA-AI) has shown improved discrimination over MELD-Na and MELD 3.0 in predicting waitlist mortality and the likelihood of delisting due to clinical deterioration (Gómez-Orellana et al., 2025). Other AI frameworks, such as optimal classification trees (OCTs), provide interpretable, data-driven insights for prioritising recipients and guiding real-time donor-recipient matching (Briceño et al., 2020).

These innovations may also help to address persistent disparities in transplant access. Studies have demonstrated that sociodemographic factors – including race, insurance status, and educational attainment – significantly affect access to both deceased and living donor liver transplantation (Lentine et al., 2023).

Monitoring and post-transplant outcomes

AI applications in post-transplant care include predictive tools for rejection, infection, and graft dysfunction (Baciu et al., 2022). Remote monitoring systems, particularly in low-resource environments, are being developed to track vital signs, medication adherence, and immunologic markers, facilitating early intervention and reducing the burden of in-person follow-up (Nwankwo et al., 2024).

Donor-derived cell-free DNA (cfDNA) has emerged as a biomarker for early graft injury, and AI-assisted platforms may improve the interpretation of cfDNA trends and thresholds for intervention (Baumann et al., 2022; Jana et al., 2024). Similarly, AI-based liver volumetry significantly reduces analysis time while enhancing reproducibility, supporting consistent surveillance across centres (Machry et al., 2023). Quantitative assessment of hepatic steatosis through automated imaging platforms further improves graft acceptance criteria and risk stratification (Narayan et al., 2022).

Global and ethical considerations

Implementing AI in liver transplantation presents unique challenges, particularly in low- and middle-income countries (LMICs). Barriers include limited access to electronic health infrastructure, insufficient clinician training in AI technologies, and data scarcity (Kimiafar et al., 2023; Nakayama et al., 2023; Farhat et al., 2024; Krones and Walker, 2024). Moreover, AI models trained on datasets lacking population diversity may inadvertently perpetuate existing healthcare inequities (Liu et al., 2019; Mehrabi et al., 2021; Shipton and Vitale, 2024).

Robust data governance is essential. Regulatory frameworks such as the General Data Protection Regulation (GDPR) mandate transparency, data minimization, and informed consent in developing and deploying AI tools (Shabani and Marelli, 2019). Additionally, the adaptive nature of AI algorithms presents difficulties in achieving regulatory approval under current frameworks, necessitating updated guidelines from bodies such as the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) (Benjamens et al., 2020). As AI becomes increasingly embedded in transplant decision-making, its ethical and operational integration will require cross-disciplinary collaboration, continuous validation, and equitable access to technological infrastructure.

Surgical and technological innovations

Recent advances in surgical technique and perioperative management have redefined the technical boundaries of liver transplantation. Innovations such as minimally invasive procedures,

Table 2: Surgical and technological innovations

Innovation (Ref.)	Description	Clinical benefit	AI integration	Current limitations
Normothermic Machine Perfusion (NMP) (Bonaccorsi-Riani et al., 2024; Karageorgos et al., 2025; Safi et al., 2025)	*Ex vivo* organ preservation under near-physiologic conditions	Improves graft viability and assessment	Ongoing development for perfusion metric analysis	Expensive and technically demanding
Robotic liver transplantation (Matsushima et al., 2025)	Minimally invasive donor/recipient surgeries using robotic systems	Reduced blood loss, faster recovery	AI used in planning and simulation	High cost and technical skill requirement
Bioengineered liver grafts (Min et al., 2017; Khalil et al., 2023)	Liver constructs using stem cells and decellularized scaffolds	Potential long-term solution for organ shortage	AI used in design and optimization	Vascularization and immune tolerance challenges
AI-guided surgical risk models (Lopez-Lopez et al., 2024)	Explainable AI models for operative complexity prediction	Improves intra-operative planning and outcomes	Uses SHAP and machine learning algorithms	Limited availability and external validation needed
Hypothermic Oxygenated Perfusion (HOPE) (Safi et al., 2025)	Cold preservation technique with oxygenation to protect grafts	Reduces ischemia-reperfusion injury	AI models being tested for function prediction	Still under clinical evaluation

AI – artificial intelligence; SHAP – SHapley Additive exPlanations

machine perfusion systems, and bioengineered grafts are increasingly supported by AI-enhanced tools that refine surgical decision-making, expand donor utilisation and improve post-transplant outcomes. These technologies reflect a broader shift toward precision surgery and data-driven organ optimisation (Table 2).

Robotic and minimally invasive techniques

Robot-assisted and laparoscopic approaches are gaining acceptance in both donor and recipient surgeries, particularly in living donor liver transplantation (LDLT) (Liu et al., 2023). These techniques have demonstrated advantages in reducing intraoperative blood loss, enhancing visualisation, and shortening postoperative recovery times (Matsushima et al., 2025). AI-supported operative planning further strengthens these benefits by predicting technical complexity and intraoperative risk.

A multicentre study applying SHAP-based explainable AI models identified an increased risk of conversion to open surgery in segment 7 and 8 resections, especially in cases with high intraoperative blood loss or prolonged duration (Lopez-Lopez et al., 2024). Such tools may prove especially valuable in resource-constrained settings where optimising surgical outcomes and operative efficiency is paramount.

Bioengineered liver grafts

Developing bioengineered livers represents a long-term solution to the persistent donor organ shortage. These constructs rely on decellularized scaffolds and repopulation with induced pluripotent stem cells (iPSCs) or primary hepatocytes, aiming to replicate native liver architecture and function (Khalil et al., 2023). A key challenge remains the complete endothelialisation of the vascular network, which is essential for graft viability and host integration (Min et al., 2017).

Parallel clinical priorities include optimizing cardiovascular risk management in LT candidates. Multidisciplinary consensus recommends preoperative coronary revascularization for asymptomatic individuals with significant stenosis and initiation of guideline-directed medical therapy (GDMT) in high-risk patients. These strategies are increasingly considered in bioengineered graft trials (Pagano et al., 2024).

Machine perfusion and organ optimization

Normothermic machine perfusion (NMP) and hypothermic oxygenated machine perfusion (HOPE) represent transformative graft preservation and evaluation technologies. These techniques allow for *ex vivo* organ assessment under physiologic or hypothermic conditions, offering real-time data on hepatocellular function, bile production, and metabolic profiles (Bonaccorsi-Riani et al., 2024; Karageorgos et al., 2025; Safi et al., 2025).

NMP, in particular, has been instrumental in expanding the use of extended criteria and donation after circulatory death (DCD) grafts. AI-integrated perfusion systems are under development to interpret perfusion metrics and predict post-transplant outcomes, potentially guiding organ acceptance decisions more reliably than static parameters alone.

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Surgical risk allocation and ethical considerations

Concerns have been raised regarding the allocation of marginal or high-risk grafts, such as DCD livers, to recipients with increased vulnerability, including those with frailty or reduced physiologic reserve (Balogh et al., 2025). Several predictive models – such as the Liver Graft Assessment Following Transplantation (L-GrAFT) score and e-GLR index – are being evaluated to facilitate more accurate preoperative assessment and equitable graft allocation (Safi et al., 2025).

The GEMA-AI model has shown superior performance in short-term mortality prediction compared to MELD-based systems and may assist transplant centers in prioritizing candidates with the highest expected benefit (Gómez-Orellana et al., 2025). As AI tools become more integrated into clinical practice, ethical safeguards must accompany their application, ensuring transparency, equitable access, and the avoidance of implicit bias in recipient selection.

Infection risk and immunosuppression

Infectious complications remain among the most common and severe threats to graft and patient survival following liver transplantation. The interplay between immunosuppression, surgical stress, and nosocomial exposure contributes to a heightened risk, particularly in the early postoperative period. Advances in preoperative risk stratification, perioperative protocols, and AI-enabled predictive tools are reshaping infection prevention strategies and informing the next generation of immunosuppressive regimens.

Preoperative screening and risk factors

Pre-transplant screening protocols now routinely include assessment for cytomegalovirus (CMV), hepatitis viruses, and colonization with multidrug-resistant organisms (MDROs), given their established role in post-transplant infectious morbidity (Sun et al., 2024; Wu et al., 2024). Clinical risk factors such as diabetes mellitus, renal insufficiency, preoperative mechanical ventilation, and use of extracorporeal detoxification systems (e.g., MARS) have been independently associated with increased risk of postoperative respiratory failure (PRF) and sepsis (Huang et al., 2011). Early extubation strategies and personalized anesthetic approaches – such as epidural analgesia – have shortened ICU (intensive care unit) stays and reduced nosocomial infection rates (Aniskevich et al., 2023; Jeon et al., 2025). These findings support an integrated approach to perioperative care, combining infection prevention with enhanced recovery pathways.

Intraoperative and early postoperative control

Intraoperative contamination and early postoperative immunosuppression create a window of heightened susceptibility to infection. Adherence to strict aseptic techniques, appropriate perioperative antibiotic prophylaxis, and rapid extubation protocols are essential to infection control. AI-based predictive models have demonstrated potential in identifying high-risk patients preoperatively, facilitating earlier intervention, and targeted antimicrobial stewardship (Hohenreuther et al., 2025).

The increasing incorporation of immunotherapeutic agents into pre-transplant cancer management – such as checkpoint inhibitors and cytokine modulators – has introduced new complexities. While these agents may improve tumour control, their immunomodulatory effects pose potential risks in the peri-transplant period and require careful monitoring and prospective evaluation (Pettas et al., 2025).

Immunosuppressive regimens and metabolic complications

Contemporary immunosuppressive protocols often combine corticosteroids, calcineurin inhibitors (CNIs), antimetabolites, and mammalian target of rapamycin (mTOR) inhibitors, each associated with distinct metabolic and infectious risks. Corticosteroids contribute to insulin resistance and dyslipidemia. CNIs such as cyclosporine and tacrolimus are linked to hypertension and post-transplant diabetes mellitus (PTDM), with tacrolimus exhibiting a relatively favourable lipid profile (Gabrielli et al., 2024). mTOR inhibitors (e.g., everolimus, sirolimus) are associated with elevated triglyceride and LDL levels, although their antiproliferative effects may benefit selected oncology patients. Antimetabolites such as azathioprine and mycophenolate mofetil are metabolically neutral but insufficient for graft protection (Gabrielli et al., 2024).

Emerging approaches – including autologous cell-based bioengineered grafts – may reduce or eliminate the need for conventional immunosuppression in the future (Khalil et al., 2023). In the interim, AI-assisted risk stratification and pharmacogenomic profiling may support individualized immunosuppression strategies that balance graft tolerance with infection risk (Basuli and Roy, 2023).

Post-transplant outcomes and complications

While advances in surgical technique, perioperative management, and immunosuppression have improved

early survival after liver transplantation, long-term outcomes remain influenced by a complex interplay of graft-related, patient-specific, and systemic factors. The focus has progressively shifted toward preventing complications, enhancing functional recovery, and identifying recurrence risk, with AI-driven tools and biomarker platforms playing an increasingly prominent role in outcome surveillance.

Graft monitoring and biomarkers

Graft function assessment has traditionally relied on biochemical markers and imaging studies; however, these modalities often lack specificity and early predictive capacity. cfDNA has emerged as a promising biomarker for subclinical graft injury and acute rejection, allowing for earlier therapeutic intervention and potentially improved graft salvage (Baumann et al., 2022; Jana et al., 2024).

AI-assisted imaging analysis has demonstrated high accuracy in identifying steatosis, vascular abnormalities, and biliary complications, thereby reducing interobserver variability and enhancing diagnostic consistency (Narayan et al., 2022; Malik et al., 2024). Furthermore, AI-based liver volumetry has significantly improved the speed and reproducibility of graft size assessments, contributing to better surgical planning and postoperative monitoring (Machry et al., 2023).

One-year patient survival rates now exceed 85% in most transplant centers, with five-year graft survival approaching 75%, although variability persists depending on donor quality, cold ischemia time, and recipient comorbidities (Bolondi et al., 2016; Strauss et al., 2022; Olawade et al., 2025).

Morbidity and mortality predictors

Frailty, renal dysfunction, and infection are the most consistent predictors of early morbidity and mortality following liver transplantation. Notably, frailty has emerged as a time-dependent risk factor, increasingly predictive of outcomes beyond the immediate postoperative period, in contrast to the MELD score, whose predictive value diminishes after transplant (Balogh et al., 2025). KPS remains the only frailty-related tool incorporated by the OPTN, but it offers limited granularity for clinical decision-making.

Recent data suggest that the APACHE IV score outperforms MELD in predicting short-term mortality in critically ill transplant recipients, offering a more dynamic and physiologically comprehensive risk assessment (Hu et al., 2013; Hamilton et al., 2021; Matsushima et al., 2025). In high-risk populations such as early liver transplant recipients with AAH, elevated infection rates and healthcare utilization highlight the need for intensified post-discharge monitoring and resource planning (Kulkarni et al., 2023).

Recurrence and surveillance

Tumour recurrence, particularly after transplantation for HCC, remains a significant concern. Recent evidence suggests that late recurrence – occurring beyond two years post-transplant – may be more common than previously recognized, necessitating extended surveillance protocols (Garas et al., 2025).

Macrovascular invasion on explant histopathology is among the strongest predictors of recurrence and is increasingly integrated into selection criteria and prognostic models (Garas et al., 2025). AI-enhanced radiologic tools and dynamic risk scoring systems incorporating biomarkers such as alpha-fetoprotein (AFP) and glypican-3 (GPC3) offer opportunities for more refined recurrence prediction and post-transplant immunosuppression adjustment (Pettas et al., 2025). As transplant oncology continues to evolve, particularly in expanding criteria and immunotherapy integration, AI-based predictive analytics may support individualized surveillance strategies and facilitate earlier interventions in high-risk recipients.

Psychosocial outcomes and patient-centred care

Liver transplantation significantly improves life expectancy and physical function, yet psychosocial outcomes often lag behind biomedical recovery. Post-transplant quality of life (QoL) is influenced by factors such as immunosuppressive side effects, fatigue, anxiety, depression, and ICU-related psychological trauma. Integrating structured frailty assessment, early mental health intervention, and digital support tools is central to advancing a patient-centred approach in transplantation medicine.

Quality of life, frailty, and recovery

Although most transplant recipients report improved physical functioning, long-term recovery is frequently hindered by persistent fatigue, sleep disturbances, and affective symptoms. These challenges are exacerbated by chronic immunosuppression and its metabolic consequences, including diabetes, dyslipidemia, and weight gain (Gabrielli et al., 2024; Xi et al., 2025). Psychological distress – ranging from adjustment disorder to post-traumatic stress symptoms – is common, particularly in patients with prolonged ICU stays or preexisting psychiatric vulnerabilities (Sun et al., 2024).

Frailty plays a pivotal role in shaping recovery trajectories. Post-transplant mortality is significantly higher among frail recipients, and emerging evidence suggests that frailty becomes more predictive of outcomes over time, surpassing traditional markers

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such as the MELD score (Balogh et al., 2025). This underscores the value of incorporating prehabilitation strategies – nutritional optimization, physical conditioning, and cognitive support – into transplant pathways to mitigate adverse outcomes.

Enhanced recovery protocols that promote early extubation and ICU bypass in suitable patients have been associated with shorter hospital stays and improved psychological well-being (Aniskevich et al., 2023). Early identification of at-risk individuals and timely psychosocial intervention can reduce complications, improve adherence, and enhance long-term satisfaction.

Digital mental health tools and AI chatbots

Artificial intelligence has recently been explored to augment psychosocial support for transplant recipients. AI-powered chatbots, such as ChatGPT and similar platforms, have shown early promise in psychiatric inpatient settings, demonstrating improvements in self-reported quality of life and user satisfaction (Melo et al., 2024). In the transplant context, these tools may serve as adjuncts to traditional care by delivering personalized education, medication reminders, and psychological support (Garcia Valencia et al., 2023).

However, concerns regarding data privacy, lack of clinical oversight, and therapeutic misconception must be addressed. The perception that AI tools can replace human clinicians may compromise safety, particularly during crises (Khawaja and Bélisle-Pipon, 2023; Casu et al., 2024). Current guidelines recommend deploying such platforms under strict ethical frameworks, with oversight from qualified mental health professionals. Overall, enhancing psychosocial recovery requires a multidimensional strategy encompassing frailty mitigation, early mental health screening, and the ethical use of digital tools. These efforts are fundamental to improving survival and the lived experience of liver transplant recipients.

Challenges, gaps, and future directions

Despite substantial advances in surgical techniques, immunosuppressive therapy, and data-driven clinical tools, liver transplantation faces significant clinical, ethical, and technological challenges. Addressing these gaps is essential to improve long-term outcomes, reduce health disparities, and optimize the full potential of emerging innovations, particularly those involving AI.

Translational barriers to AI implementation

One of the foremost obstacles to the clinical integration of AI in transplantation is the limited availability of large, high-quality, and diverse datasets. Most current models are trained on retrospective, single-center data that may not generalize across populations, increasing the risk of algorithmic bias and poor external validity (Machry et al., 2023; Krones and Walker, 2024; Singhal et al., 2024). This issue is particularly acute in low- and middle-income countries (LMICs), where electronic health records are fragmented or absent, and AI literacy among clinicians is limited (Nakayama et al., 2023; Farhat et al., 2024; Krones and Walker, 2024).

Furthermore, many AI systems are "black boxes", offering limited interpretability and raising concerns regarding transparency and clinical accountability. Adaptive learning algorithms, which evolve based on new inputs, present additional challenges to current regulatory frameworks. Agencies such as the FDA and EMA are developing guidelines for such tools, but comprehensive regulatory infrastructure remains under development (Benjamens et al., 2020).

Data privacy and compliance with international standards such as the GDPR are essential to maintain patient trust and institutional integrity. Appropriate consent procedures must accompany the ethical deployment of AI tools, transparent disclosure of model limitations, and equitable representation of patient subgroups (Liu et al., 2019; Shabani and Marelli, 2019; Mehrabi et al., 2021).

Innovative frontiers and multidisciplinary integration

Integrating AI with other transformative technologies offers exciting possibilities as the field moves forward. AI-guided genome editing using CRISPR holds promise for tailoring immunologic compatibility and reducing reliance on long-term immunosuppression. AI models may assist in identifying immunogenic variants. At the same time, CRISPR-based techniques could be employed to modify relevant genetic loci in donor or recipient cells, though these applications remain largely theoretical (Dixit et al., 2024).

Open-access AI platforms and federated learning models could address equity concerns by enabling secure, decentralized training across multiple institutions (Ritoré et al., 2024). Such approaches may democratize access to transplant innovations, particularly in resource-limited settings (Machry et al., 2023). In parallel, cost-effective tools such as LiverColor for hepatic steatosis assessment or smartphone-based diagnostic platforms are expanding the reach of AI into underserved regions (Gómez-Gavara et al., 2024).

Additional clinical gaps include the need for validated frailty-specific scoring systems, improved utilization of marginal grafts, and refined strategies for long-term

surveillance and immunosuppression personalization. For example, phosphatidyl ethanol (PEth) has emerged as a reliable biomarker for alcohol use monitoring, particularly in recipients transplanted for alcohol-associated liver disease (Sharma et al., 2024). Similarly, tumour-specific markers such as AFP and GPC3, when integrated with AI-enhanced imaging, may improve transplant oncology outcomes (Pettas et al., 2025; Sha et al., 2025).

Disparities in access to deceased and living donor organs persist across demographic and socioeconomic strata, underscoring the need for policies that explicitly incorporate equity metrics into allocation algorithms (Strauss et al., 2022; Lentine et al., 2023). Moreover, structured psychological support for living donors remains inadequately addressed and warrants systematic implementation (Lee et al., 2025).

Advancing the next generation of transplant medicine will require cross-disciplinary collaboration among transplant surgeons, hepatologists, ethicists, data scientists, and policymakers. By aligning technical innovation with clinical pragmatism and ethical responsibility, the field is poised to redefine what is achievable in liver transplantation.

Conclusion

Liver transplantation continues evolving as a multidisciplinary endeavor integrating surgical precision, immunological management, and emerging technological advances. While considerable progress has been made in short- and intermediate-term survival, persistent challenges – including organ scarcity, post-transplant complications, and health disparities – highlight the need for ongoing innovation and systemic reform.

AI has emerged as a promising adjunct to traditional clinical decision-making, offering enhancements in diagnostic imaging, graft assessment, surgical planning, and postoperative surveillance. As these tools mature, their potential to improve risk stratification, personalize immunosuppression, and streamline organ allocation will depend on rigorous validation, equitable implementation, and ethical oversight.

Equally important is recognizing that patient-centred outcomes – such as quality of life, psychosocial recovery, and functional independence – are essential to defining transplant success. Addressing frailty, optimizing prehabilitation, and supporting post-transplant mental health must become integral components of comprehensive transplant care.

Future directions should focus on fostering cross-disciplinary collaboration, developing inclusive and representative datasets, and supporting scalable solutions applicable across diverse clinical and geographic contexts (Korylchuk et al., 2024). As liver transplantation enters the era of precision medicine, integrating ethical, technological, and clinical frameworks will be critical to ensuring that innovation translates into equitable and durable improvements in patient outcomes.

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