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"Machine Perfusion for Liver Preservation: Technologies and Translational Advances"

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Abstract

Liver transplantation remains the definitive treatment for end-stage liver disease; however, preservation strategies critically influence graft viability and post-transplant outcomes. Conventional static cold storage (SCS) is limited by the inability to provide metabolic support or assess organ function prior to transplantation. Machine perfusion (MP) has emerged as a transformative technology enabling continuous oxygenation, nutrient delivery, and real-time viability assessment. This review evaluates the current state of liver perfusion technologies, including hypothermic, subnormothermic, and normothermic perfusion approaches. A structured literature analysis was performed to assess technological evolution, clinical outcomes, and regulatory considerations. Key findings indicate that MP improves graft utilization, reduces ischemia-reperfusion injury, and enables functional assessment through biomarkers such as lactate clearance, bile production, and mitochondrial indicators. Reported clinical benefits include reduced biochemical graft injury, reduced post-transplant AST/ALT release in selected studies, improved lactate clearance, increased bile production, lower early allograft dysfunction, extended preservation time, and improved utilization of extended criteria donor livers. Despite promising outcomes, challenges remain in standardization, cost, infrastructure requirements, training, and integration into clinical workflows. Future directions include multi-modal perfusion strategies, real-time metabolic sensing, biosensor integration, artificial intelligence-based viability prediction, and portable perfusion systems for broader clinical adoption. This review provides a comprehensive overview of current technologies and highlights pathways for translational advancement.

Keywords: Machine perfusion, Liver preservation, Normothermic perfusion, Hypothermic perfusion, Organ viability, Transplantation, Ex vivo perfusion, Ischemia-reperfusion injury

Introduction

Background and Epidemiological Context

Liver transplantation is the gold standard for treating end-stage liver disease, yet donor organ shortage remains a major global challenge. Static cold storage (SCS), the conventional preservation method, limits preservation time and does not allow functional assessment prior to implantation [1,2]. Global liver transplantation activity has increased over the last decade; however, demand continues to exceed available donor organs. The Global Observatory on Donation and Transplantation reported 42,497 liver transplants worldwide in 2024, with approximately 23% performed using living donors [8]. In 2021,

approximately 34,944 liver transplants were performed globally, again illustrating the substantial worldwide need for transplant services [9]. Despite this activity, many patients remain on waiting lists or experience waitlist dropout because suitable organs are not available in time.

Organ discard remains a clinically important issue, particularly for donor livers considered marginal because of steatosis, donor age, donation after circulatory death (DCD), prolonged ischemia time, or uncertain functional quality. Extended criteria donor (ECD) grafts are increasingly used to address organ shortage, but they carry higher risk of ischemia-reperfusion injury, early allograft dysfunction, and biliary complications. Machine perfusion has therefore gained importance because it can preserve, assess, and potentially recondition these grafts before transplantation, thereby improving organ utilization and reducing unnecessary discard [3,8-10].

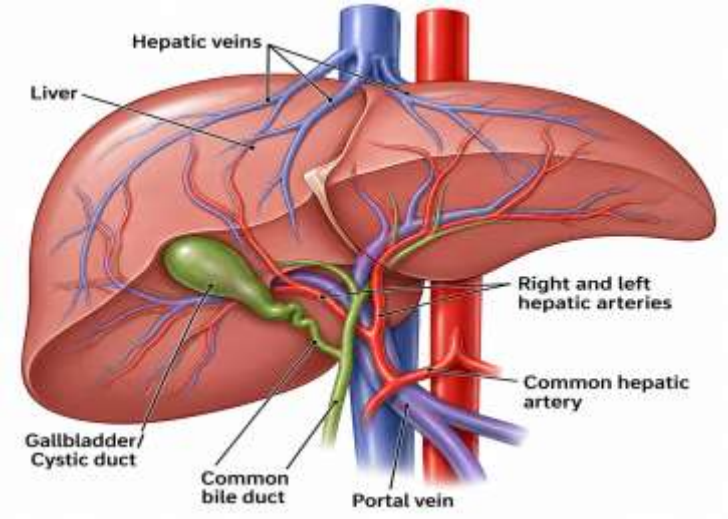

Figure 1: Dual perfusion physiology of the liver (29)

The liver receives approximately 70-75% of its blood supply from the portal vein (low pressure, high flow) and approximately 25-30% from the hepatic artery (high pressure, oxygen-rich). The peribiliary plexus is primarily supplied by the hepatic artery, making arterial perfusion critical for biliary integrity. This dual inflow is essential to maintain sinusoidal perfusion and prevent ischemic injury [5,6].

Clinical Relevance of Dual Blood Supply

The liver is uniquely susceptible to preservation injury because its parenchymal and biliary structures depend on coordinated portal venous and hepatic arterial inflow. Portal venous perfusion maintains bulk sinusoidal flow, whereas hepatic arterial perfusion provides oxygen-rich blood to the bile ducts through the peribiliary plexus. Disruption of hepatic arterial flow can therefore aggravate ischemia-reperfusion injury, impair cholangiocyte oxygenation, and increase the risk of biliary complications, including ischemic cholangiopathy after transplantation [6,7,11].

Need for Review

Recent advancements in machine perfusion have introduced multiple preservation strategies; however, variability in perfusion temperature, perfusate composition, device configuration, and viability criteria necessitates a consolidated evaluation of current technologies and clinical evidence [2,3].

Objective

- Evaluate existing liver perfusion technologies
- Compare different perfusion strategies
- Analyze clinical and regulatory landscapes
- Summarize measurable outcomes and viability thresholds from key studies
- Identify future directions for innovation

Although liver machine perfusion is primarily a transplantation technology, its development relies heavily on biomedical engineering, fluid management systems, sensor technologies, automation, and digital health integration. From a medical device perspective, this field represents a significant opportunity for the development of next-generation organ preservation platforms capable of providing controlled perfusion, real-time metabolic monitoring, and data-driven viability assessment.

As a medical technology organization, retaining expertise in precision engineering, extracorporeal systems, biomaterials, sterile disposable devices, and integrated sensing technologies may contribute to the advancement of scalable and clinically deployable organ preservation systems. This review was therefore undertaken to identify current technological gaps, future innovation opportunities, and potential translational pathways that may support the development of safer, more efficient, and more objective organ preservation solutions.

Methodology

Literature Search Strategy

A structured narrative literature review was conducted using PubMed, Scopus, and Google Scholar to identify relevant clinical studies, preclinical investigations, review articles, regulatory documents, and patents related to liver machine perfusion. Search terms included “liver perfusion,” “normothermic machine perfusion,” “hypothermic perfusion,” “hypothermic oxygenated perfusion,” “organ preservation,” “ex vivo liver perfusion,” “ischemia-reperfusion injury,” “ischemic cholangiopathy,” “extended criteria donor,” “lactate clearance,” “bile production,” “flavin mononucleotide,” and “transplant viability biomarkers.” Studies were selected based on relevance to perfusion technology, clinical outcomes, viability assessment, perfusion parameters, and translational applicability.

The literature search was conducted between January 2016 and March 2026. Seminal studies published before 2016 were additionally identified through manual screening of reference lists where relevant. A total of 87 records were initially identified through database searches. After removal of duplicates and screening of titles and abstracts, 42 full-text articles were assessed for eligibility. Ultimately, 30 studies meeting predefined inclusion criteria were incorporated into the review. The study selection process followed PRISMA recommendations to improve methodological transparency and minimize selection bias. These numbers should be verified against the final database search log before journal submission.[5,6]

Selection Criteria

Included studies comprised clinical trials, preclinical studies, review articles, regulatory documents, and relevant technological reports. Studies without perfusion outcome data, non-peer-reviewed commentary without technical relevance, and articles not directly related to liver preservation were excluded.

Data Extraction

Data extracted included perfusion mode, temperature range, flow and pressure parameters, viability markers, biomarker thresholds, clinical outcomes, graft survival data, device characteristics, approval status, portability, cost considerations, infrastructure requirements, and limitations.

Literature Review

Current State of the Art

Table 1: Overview of Existing Devices and Technologies

Device	Perfusion type	Temperature range	Clinical approval / regulatory status	Portability
Device 1	Normothermic machine perfusion	Near physiological, approximately 35-37°C	Transportable device; FDA documentation describes intended use for donor liver normothermic perfusion and preservation; approval/indications vary by jurisdiction [12]	Transportable, not certified for air transport in the US IFU [12]
Device 2	Portable normothermic perfusion and monitoring	Near physiological, approximately 35-37°C	FDA PMA approved for selected DBD and DCD donor livers; CE marked [13,14]	Portable extracorporeal organ perfusion platform [13]
Device 3	Hypothermic, oxygenated, subnormothermic, and normothermic configurations depending on protocol	Approximately 4-37°C depending on HMP, HOPE, SNMP, or NMP protocol	Used clinically and in research settings; approval status varies by region [15]	Portable/transportable system configurations available

Technological Advancements

- Normothermic perfusion (NMP) for functional assessment
- Hypothermic oxygenated perfusion (HOPE) for mitochondrial protection
- Controlled oxygenated rewarming (COR) to reduce reperfusion injury
- Real-time metabolic monitoring and biosensor integration
- Artificial intelligence-based viability prediction and decision support

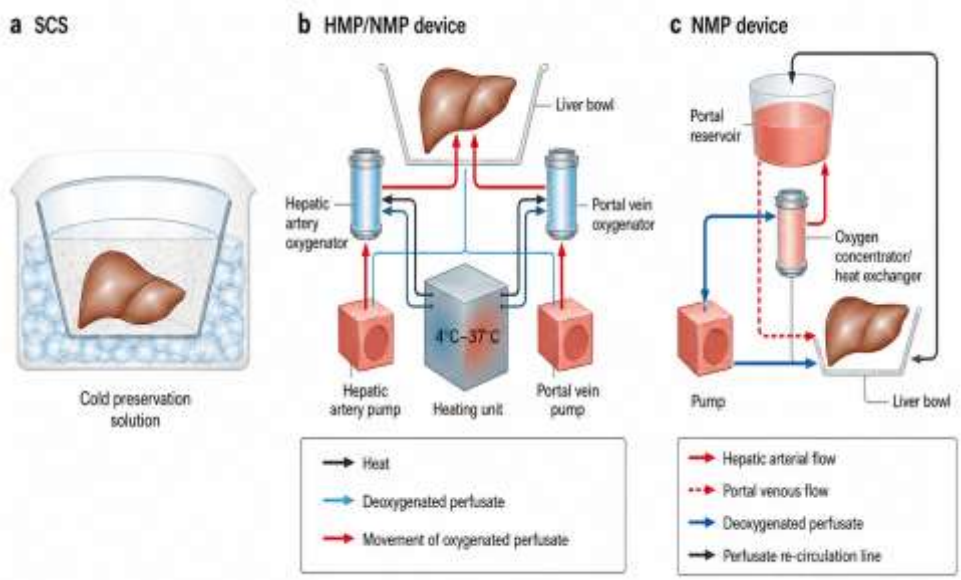

Figure 2: Temperature-dependent metabolic modulation in machine perfusion [30]

Hypothermic perfusion (4-10°C) reduces metabolic demand and preserves ATP, while normothermic perfusion (36-37°C) restores physiological metabolism, enabling functional assessment. Subnormothermic perfusion provides intermediate metabolic activity and may reduce ischemia-reperfusion injury [3,4].

Studies demonstrate reduced AST/ALT levels, improved bile production, lower early allograft dysfunction, longer preservation time, and improved early graft function in selected clinical contexts [3,5-7,16-18].

Major Clinical Studies and Outcomes

Clinical studies have demonstrated that machine perfusion provides measurable benefits over static cold storage by improving graft assessment, reducing preservation-related injury, and increasing utilization of marginal donor organs. In the randomized trial by Nasralla et al., normothermic machine perfusion was associated with approximately 50% lower graft injury, approximately 50% lower organ discard, and approximately 54% longer mean preservation time compared with static cold storage [3]. The protect trial and real-world experience with normothermic perfusion have also reported reduced early allograft dysfunction and longer preservation windows in selected donor liver cohorts [16,17].

Hypothermic oxygenated perfusion has been associated with mitochondrial protection, improved ATP recovery, reduced flavin mononucleotide release, and reduction of ischemia-reperfusion-related injury. These effects are particularly relevant for extended criteria and DCD grafts, which are more vulnerable to mitochondrial dysfunction and biliary complications [5,11,18].

Table 2: Clinical Outcomes, Survival Impact, Cost, and Limitations of Liver Machine Perfusion Strategies

Study / Reference	Perfusion strategy	Clinical outcomes	Graft survival differences	Cost considerations	Limitations
Nasralla et al.,	NMP	Lower graft	No major	Higher device	Requires

2018 [3]		injury, lower discard, longer preservation time	difference in patient/graft survival reported in the trial period	and disposable cost than SCS	trained staff, perfusion logistics, and device availability
Guarrera et al., 2010 [6]	HMP	Reduced biochemical evidence of hepatocellular injury; improved early graft function parameters	Limited early clinical series, not powered for long-term survival differences	Lower complexity than NMP but still requires equipment and disposables	Limited functional metabolic assessment compared with NMP
Watson et al., 2018 [7]	NMP for assessment of donor livers	Lactate clearance, bile production, pH, vascular flow, and hemodynamic stability used as viability indicators	Useful for graft selection; survival depends on donor/recipient factors	Cost may be justified if marginal graft use increases	Viability criteria vary across centers
Schlegel et al., 2015 [5]	HOPE	Mitochondrial protection and reduced reperfusion injury	Potential benefit in ECD/DCD grafts	Moderate cost relative to SCS; generally simpler than NMP	Limited immediate full metabolic assessment
Mergental et al., 2020 [10]	NMP viability testing of discarded livers	Successful transplantation of 71% of previously discarded livers; 100% 90-day patient and graft survival in the study cohort	Excellent short-term survival in selected cohort	Potentially offsets cost by increasing organ utilization	Small/selected cohort and persistent risk of biliary complications in some DCD grafts

Regulatory and Clinical Landscape

- Several liver perfusion systems have obtained regulatory clearance or approval in major markets; however, indications and requirements vary by jurisdiction.
- Clinical trials have demonstrated improved graft utilization, lower graft injury, and longer preservation time in selected settings.

- Regulatory challenges include classification of combination systems, validation of viability markers, device training requirements, and cost-effectiveness demonstration.

Mechanism of Action and Design Considerations

Design Principles

- Dual perfusion through the portal vein and hepatic artery
- Pressure-controlled arterial flow and low-pressure portal venous flow
- Temperature-controlled organ chamber and perfusate circuit
- Oxygenator, reservoir, pump module, filters/bubble traps, and sensors
- Real-time monitoring of pressure, flow, temperature, oxygenation, and biochemical markers

Inadequate hepatic arterial perfusion is clinically important because the biliary epithelium depends heavily on arterial oxygen supply. During procurement, preservation, and reperfusion, disruption of arterial inflow can intensify ischemia-reperfusion injury, reduce oxygen delivery to the peribiliary plexus, and contribute to ischemic cholangiopathy, non-anastomotic biliary strictures, and graft dysfunction. Therefore, dual inflow control is not only an engineering feature but also a clinically relevant requirement for liver graft protection [6,7,11].

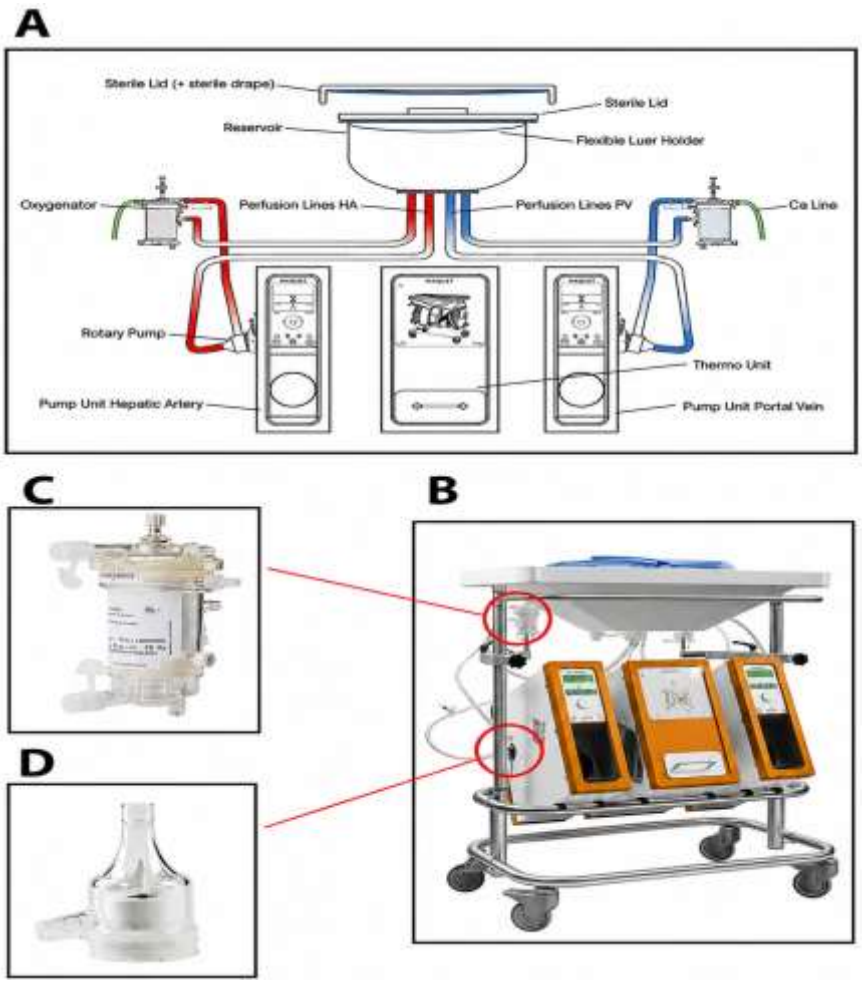

Figure 3: Representative configuration of a dual-perfusion ex vivo liver perfusion system and key circuit components [31]

Dual inflow through the hepatic artery and portal vein, integrated oxygenator, reservoir, pump, organ chamber, temperature control, arterial filter/bubble trap, and monitoring sensors. [1]

Performance and Efficacy

Performance is evaluated using hemodynamic parameters, biochemical markers, functional outputs, and organ appearance. Common parameters include:

- HA pressure: 50-100 mmHg
- PV pressure: 3-10 mmHg
- HA flow: 150-700 mL/min
- PV flow: 950-1750 mL/min [4,6]

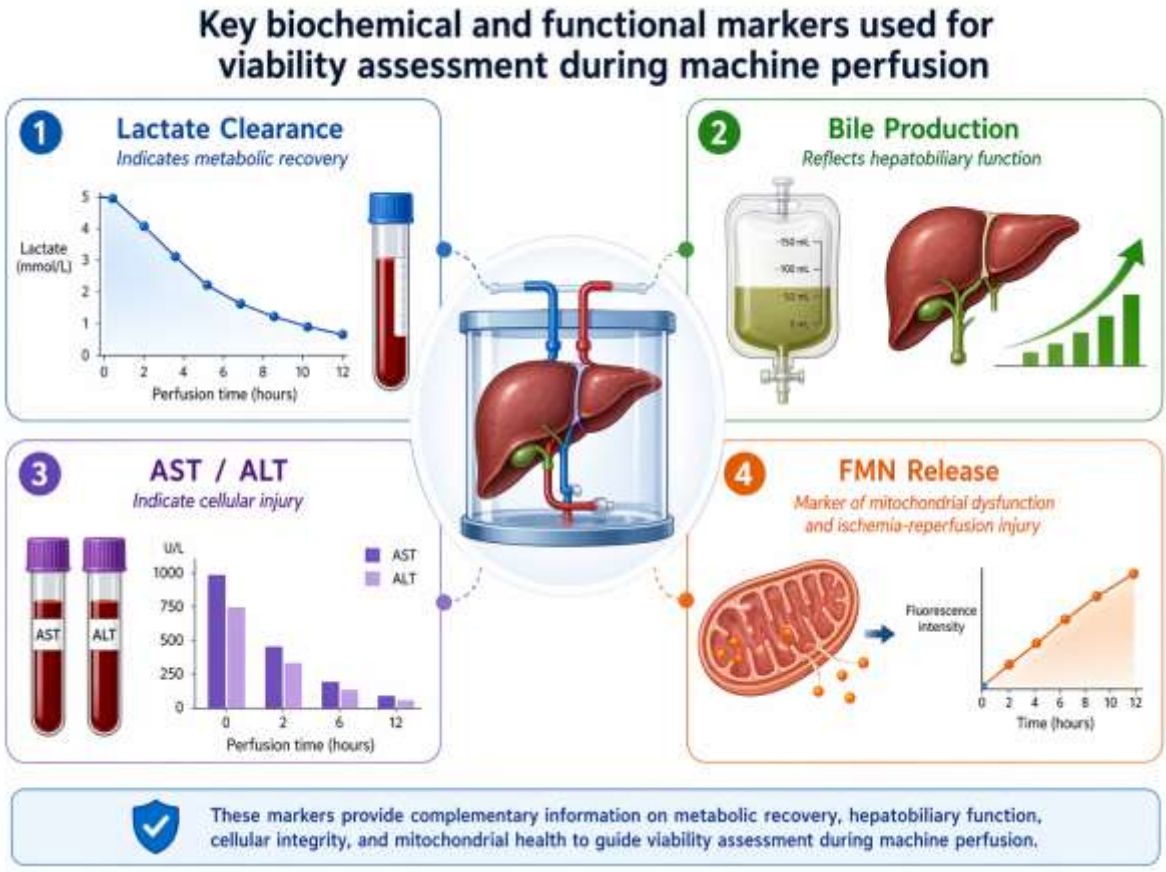

Figure 4: Key biochemical and functional parameters used to assess donor liver viability during machine perfusion. Lactate clearance serves as an indicator of metabolic recovery and adequate hepatocellular function. Bile production reflects hepatobiliary activity and biliary epithelial integrity. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels are commonly used markers of hepatocellular injury. Flavin mononucleotide (FMN) release has emerged as a marker of mitochondrial dysfunction and ischemia–reperfusion injury. Figure created by the authors using artificial intelligence-assisted illustration based on published literature. [7, 8, 9, 10]

Clinical Interpretation of Biomarkers and Thresholds

Biomarker interpretation should be based on combined trends rather than a single value. Thresholds vary between centers and protocols; therefore, the following values should be considered commonly reported criteria rather than universal acceptance criteria.

Table 3: Clinical Interpretation of commonly reported threshold biomarkers:

Biomarker / Parameter	Commonly reported threshold or criterion	Clinical interpretation
Lactate clearance	Perfusate lactate <2.5 mmol/L within 2-4 hours of NMP is widely used in viability protocols [19-22]	Indicates restoration of hepatic metabolic function and adequate oxygen-dependent lactate metabolism
Bile production	Any bile production is a major positive sign; some protocols use cumulative bile production >25 mL with bile pH >7.5 and bile bicarbonate >25 mmol/L [20,21]	Reflects hepatobiliary function and cholangiocyte activity
AST/ALT	No universal acceptable range; falling or stable trends are preferred. Some protocols use ALT <6,000 IU/L as an acceptance criterion [20,21]	High or rising transaminases suggest hepatocellular injury and poor graft quality
Perfusate pH	Perfusate pH >7.20-7.30 is commonly used with other criteria [20,21]	Maintained pH suggests preserved metabolic regulation and adequate perfusion
Flow and vascular resistance	Stable HA flow >150 mL/min and PV flow >500 mL/min have been used in viability protocols [21]	Indicates acceptable vascular resistance and sinusoidal perfusion
FMN	No universally accepted cutoff; assay-specific thresholds are under validation [18,23,24]	FMN is released from mitochondrial complex I and reflects mitochondrial injury, ischemia-reperfusion risk, cholangiopathy risk, and graft loss prediction

Machine perfusion allows continuous assessment of both vascular and metabolic performance. Stable hepatic artery and portal vein flows indicate preserved vascular resistance and adequate sinusoidal perfusion. Lactate clearance is commonly used as a marker of metabolic recovery, while bile production reflects hepatobiliary function. AST and ALT release indicate hepatocellular injury, whereas FMN release provides information regarding mitochondrial dysfunction and ischemia-reperfusion injury. Therefore, hemodynamic stability, improving metabolic markers, controlled perfusate pH, bile production, and low injury-marker release together provide a more reliable assessment of graft viability than any single parameter alone.

Table 4: Comparative Analysis

Parameter	Static Cold Storage	Hypothermic Machine Perfusion	Normothermic Machine Perfusion
Temperature range	0-4°C	4-12°C	35-37°C
Metabolic activity	Minimal	Low	Near physiological
Oxygen delivery	No active oxygenation	Possible with oxygenated HMP/HOPE	Continuous oxygenation
Nutrient delivery	No	Limited	Yes
Functional assessment	Not possible	Limited biochemical and mitochondrial assessment	Real-time metabolic and functional assessment
Key markers	Cold ischemia time only	FMN, perfusate enzymes, vascular resistance	Lactate clearance, bile production, pH, AST/ALT, flow, pressure
Clinical outcomes	Established but limited for marginal grafts	Reduced ischemia-reperfusion injury in selected grafts	Reduced graft injury, lower EAD in selected studies, longer preservation time
Graft survival differences	Baseline comparator	Potential benefit in ECD/DCD grafts; long-term benefit still under evaluation	No universal survival advantage, but improved assessment and early outcomes reported
Cost considerations	Lowest cost; standard cold storage materials	Moderate equipment/disposable cost	Highest equipment/disposable cost and staff requirement
Main advantage	Simple and low cost	Reduces ischemia-reperfusion injury and mitochondrial injury	Enables viability testing and marginal graft assessment
Main limitation	No active support or viability testing	Limited metabolic assessment	Higher cost and technical complexity
Clinical adoption	Established standard	Increasing	Rapidly expanding in specialized centers

Cost, Infrastructure and Training Considerations

Cost remains one of the major barriers to widespread implementation of liver machine perfusion. Unlike SCS, machine perfusion requires a console or perfusion platform, single-use sterile disposable circuits, oxygenators, tubing sets, sensors, perfusate components, blood products for NMP protocols, maintenance, quality checks, and trained personnel. The overall cost varies by country, device type,

procurement model, organ transport workflow, and whether perfusion is performed at the donor hospital, transplant center, or a regional hub.

Table 5: Cost Analysis

Cost / implementation factor	HMP / HOPE	NMP
Capital equipment	Moderate to high; depends on device configuration	High; automated NMP platforms are generally more expensive than HMP systems
Disposable circuit cost	Sterile tubing, oxygenator or perfusion set, sensors, cannulas	Single-use perfusion set, oxygenator, sensors, tubing, organ reservoir, filters, and blood-based perfusate components
Infrastructure	Perfusion area, oxygen supply, cold-chain support, sterile setup, trained transplant/perfusion staff	Perfusion area, blood bank support, gas supply, temperature control, biochemical monitoring, transport logistics, and continuous supervision
Training	Training in priming, cannulation, pressure/flow monitoring, troubleshooting, and aseptic handling	Dedicated training for setup, priming, viability assessment, alarm response, biochemical interpretation, and emergency conversion to cold storage
Economic benefit	Potentially reduces graft injury and complications in selected grafts	Potentially increases organ utilization, reduces discard, extends preservation time, and improves logistics; cost-effectiveness depends on local program volume and outcomes

Published cost-utility analyses suggest that NMP can be cost-effective under selected willingness-to-pay thresholds, particularly when it increases transplantable organ utilization and reduces downstream complications [25]. However, in low- and middle-resource settings, high capital cost, recurring disposable cost, and lack of trained personnel may limit adoption unless simplified, portable, and cost-efficient platforms become available.

Challenges and Limitations

Although machine perfusion has shown promising clinical results, several limitations remain within the current evidence base. Available studies differ substantially in perfusion duration, perfusate composition, temperature strategy, oxygenation method, and viability assessment criteria, making direct comparison between studies challenging. In addition, key clinical endpoints such as graft survival, early allograft dysfunction, biliary complications, ischemic cholangiopathy, and organ utilization are influenced by multiple factors, including donor quality, recipient condition, surgical technique, and

center-specific transplant protocols. Furthermore, much of the available evidence is derived from single-center experiences, observational studies, or early clinical trials with relatively small sample sizes and limited long-term follow-up.

This review also has inherent limitations. Despite a structured literature search, relevant studies may have been missed due to database selection, search strategy constraints, language restrictions, or publication bias. As a narrative review, it is also subject to potential selection and interpretation bias. Additionally, the heterogeneity of the included studies limited the ability to perform direct comparisons and draw definitive conclusions regarding the superiority of one machine perfusion strategy over another. Rapid advancements in machine perfusion technologies and evolving viability assessment protocols may further limit the long-term applicability of some findings presented in this review. Therefore, future multicenter studies with standardized viability thresholds, harmonized outcome measures, and extended follow-up are required to establish robust evidence and define the most reliable clinical endpoints for machine perfusion in liver transplantation.

Technical Challenges

- Maintaining stable perfusion parameters
- Optimization of controlled additive infusion ratios
- Managing oxygenation and temperature control
- Reliable sensor calibration and real-time data interpretation
- Adaptability of the system across different clinical and geographic settings

Clinical Challenges

- Lack of universally accepted viability criteria
- Variability in clinical protocols
- Need for trained perfusion and transplant staff
- Risk of over-reliance on isolated biomarker thresholds without considering overall graft assessment

Regulatory Barriers

- Classification complexity for device-perfusate-biologic combinations
- Requirement for clinical validation
- Post-market performance monitoring
- Cost-effectiveness and reimbursement evidence requirements

Future Perspectives

Future progress in liver machine perfusion is expected to come from the integration of engineering innovation, biological monitoring, and data-driven decision support. Key emerging areas include artificial intelligence-based viability prediction, real-time metabolic monitoring, biosensor integration, and portable perfusion platforms.

Artificial Intelligence-Based Viability Prediction

AI models may combine continuous perfusion data, donor characteristics, ischemia time, perfusate biochemistry, lactate kinetics, bile composition, oxygen consumption, FMN release, and hemodynamic

trends to generate objective viability scores. Such models could reduce inter-center variability, support marginal graft acceptance decisions, and help predict early allograft dysfunction or biliary complications. However, AI tools will require multicenter datasets, external validation, explainability, and regulatory oversight before routine clinical use.

Real-Time Metabolic Monitoring and Biosensor Integration

Future perfusion systems may include inline sensors for lactate, glucose, pH, electrolytes, oxygen consumption, bile quality, inflammatory mediators, and mitochondrial injury markers such as FMN. Continuous biosensor monitoring would allow dynamic assessment of graft recovery rather than relying on intermittent sampling. Integration of sensor dashboards with automated alarms may improve clinical workflow and reduce operator-dependent variability.

Portable and Multi-Mode Perfusion Platforms

Portable systems may expand access to machine perfusion by supporting donor-hospital perfusion, transport perfusion, and hub-and-spoke transplant models. Multi-mode platforms combining hypothermic, subnormothermic, controlled rewarming, and normothermic perfusion may allow temperature-tailored preservation strategies. These systems could improve preservation flexibility, reduce cold ischemia, and support ECD and DCD graft utilization in geographically diverse settings.

Discussion

Machine perfusion represents a major transition from passive organ storage to active organ preservation, assessment, and potential reconditioning. Its clinical value is strongest in settings where donor organs are marginal, cold ischemia time is prolonged, or graft viability is uncertain. By allowing continuous oxygenation, controlled perfusion, biochemical monitoring, and functional assessment, MP may improve surgeon confidence in accepting ECD and DCD livers and may reduce unnecessary organ discard.

Implementation remains challenging. High capital investment, disposable circuit costs, blood-based perfusate requirements, oxygen supply, laboratory monitoring, maintenance, sterility assurance, and trained personnel are major adoption barriers. High-volume transplant centers may absorb these costs more easily because improved organ utilization and reduced complications can offset expenditure. In contrast, low-volume or resource-constrained centers may require shared regional perfusion hubs, simplified platforms, service-based business models, or government-supported reimbursement pathways.

Infrastructure requirements differ between technologies. HMP and HOPE are generally less metabolically complex and may be easier to implement, while NMP requires more intensive monitoring, trained operators, blood product handling, biochemical interpretation, and emergency protocols. Staff training should include device setup, priming, cannulation, pressure-flow control, troubleshooting, viability interpretation, documentation, and aseptic handling. Without adequate training, the clinical benefit of MP may be reduced by technical error or inconsistent decision-making.

The impact of hepatic arterial perfusion deserves special emphasis. The bile ducts receive most of their oxygen supply through the hepatic artery and peribiliary plexus. Therefore, disrupted arterial perfusion during retrieval, preservation, or reperfusion can worsen cholangiocyte ischemia, intensify ischemia-reperfusion injury, and contribute to ischemic cholangiopathy and non-anastomotic biliary strictures. Machine perfusion systems that support stable hepatic arterial pressure and flow may help reduce these

risks, especially in DCD and ECD grafts. However, long-term biliary outcomes remain an important endpoint for future studies.

Overall, the adoption of liver machine perfusion should be guided by clinical indication, donor risk profile, local infrastructure, cost-effectiveness, trained staff availability, and regulatory requirements. Continued standardization of viability criteria and incorporation of recent biomarkers such as FMN may help improve consistency across transplant programs.

Conclusion

Machine perfusion has emerged as a promising and rapidly evolving advancement in liver preservation, shifting the paradigm from passive cold storage toward active organ maintenance, viability assessment, and potential graft reconditioning. By providing continuous oxygenation, metabolic support, and real-time functional monitoring, machine perfusion technologies have demonstrated the potential to improve graft utilization, reduce preservation-related injury, and facilitate the use of extended criteria donor organs.

Nevertheless, widespread implementation remains limited by the absence of standardized perfusion protocols, variability in viability assessment criteria, infrastructure requirements, and high operational costs. Future progress will depend on robust multicenter clinical validation, harmonization of biomarker thresholds, and the integration of emerging technologies such as biosensors, artificial intelligence, and portable perfusion platforms.

From a translational engineering perspective, liver machine perfusion represents an important opportunity for the development of next-generation medical devices that combine fluid management, sensor technologies, automated control systems, and data-driven decision support. Such innovations may enable more objective, reproducible, and scalable organ preservation strategies.

Overall, machine perfusion has the potential to significantly enhance liver transplantation outcomes; however, continued interdisciplinary collaboration among clinicians, biomedical engineers, and medical device manufacturers are ongoing to establish safe, standardized, and economically sustainable solutions for routine clinical practice.

Hence, "This review identifies current technological gaps and future opportunities for the development of next-generation medical devices, thereby supporting translational research and innovation within the healthcare ecosystem."

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