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Review Article

Recent Advances in the Management of Liver Cirrhosis: From Non-Invasive Risk Stratification to Precision and Regenerative Therapies

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ABSTRACT

Liver cirrhosis is the advanced structural and functional consequence of chronic liver injury and is characterized by fibrosis, regenerative nodules, portal hypertension and progressive loss of hepatic reserve. The thesis on which this review is based identifies alcohol-associated liver disease, chronic hepatitis B and C, metabolic dysfunction-associated steatotic liver disease (MASLD), autoimmune disorders, inherited metabolic disease and toxic injury as major etiological pathways, and emphasizes the transition from relatively invasive diagnosis and complication-based treatment toward non-invasive risk stratification, prevention of decompensation and individualized care. Current evidence supports a stage-based model in which compensated advanced chronic liver disease is identified using non-invasive tests and clinically significant portal hypertension (CSPH) is treated before first decompensation where appropriate. Contemporary management combines elimination or suppression of the underlying cause, nutritional and lifestyle intervention, prevention of portal-hypertension complications, treatment of ascites and hepatic encephalopathy, surveillance for hepatocellular carcinoma (HCC), and timely liver-transplant evaluation. Major advances include transient and spleen-stiffness assessment, broader use of non-selective beta-blockers, refined TIPS selection, improved management of ascites and hepatorenal syndrome, highly effective antiviral therapy, and increasingly sophisticated transplantation pathways. Emerging approaches—including microbiome-directed therapy, disease-modifying antifibrotic strategies, extracellular vesicles, stem-cell and organoid platforms, artificial liver support, artificial intelligence and precision medicine—are promising but remain heterogeneous in clinical maturity. The 2026 Baveno VIII consensus further strengthens non-invasive risk stratification and prevention of decompensation. This review integrates the thesis material with recent evidence and distinguishes established clinical practice from investigational approaches, with emphasis on clinically relevant advances and future directions.

Keywords: Liver Cirrhosis; Portal Hypertension; Clinically Significant Portal Hypertension; Ascites; Hepatic Encephalopathy; Non-Invasive Tests; TIPS; Liver Transplantation; Antifibrotic Therapy; Precision Medicine; Artificial Intelligence.

Introduction

Cirrhosis is not a single disease but a final common pathway of persistent hepatic injury arising from multiple etiologies. The thesis describes cirrhosis as replacement of normal liver tissue by fibrotic scar tissue and regenerative nodules, producing architectural distortion and progressive impairment of metabolism, detoxification, bile handling and protein synthesis. These changes are clinically important because the disease can remain clinically silent for years and then transition to decompensation, marked by ascites, hepatic encephalopathy or portal-hypertensive gastrointestinal bleeding. The thesis similarly emphasizes jaundice, edema, pruritus, nutritional decline and HCC as important manifestations and complications [1].

The global burden remains substantial. WHO reports that viral hepatitis B and C caused an estimated 1.3 million deaths from related cirrhosis and liver cancer in 2024, demonstrating the continuing importance of prevention, diagnosis and access to curative or suppressive antiviral therapy [2]. At the same time, metabolic liver disease and alcohol-associated liver disease are increasingly important drivers of advanced chronic liver disease. The therapeutic landscape has consequently shifted from treating the consequences of cirrhosis to preventing the first decompensation event and, when possible, modifying the disease process itself.

The present review discusses recent advances in the management of liver cirrhosis with specially consideration to non-invasive risk stratification to precision and regenerative therapies.

Etiology and Pathobiology

The major etiologies identified in the thesis include chronic alcohol exposure, HBV and HCV infection, fatty liver disease, autoimmune liver disease, inherited metabolic disorders, biliary disease, drugs and toxins [3]. The relative contribution of each cause varies geographically and over time. Importantly, multiple etiologies may coexist; for example, metabolic dysfunction, alcohol exposure and viral hepatitis can interact to accelerate fibrosis.

Cirrhosis develops through persistent hepatocellular injury, inflammatory signaling, extracellular-matrix deposition and progressive remodeling of the sinusoidal and vascular compartments. Hepatic stellate cells are central effector cells: when activated by inflammatory and oxidative signals, they acquire a myofibroblast-like phenotype and produce collagen and other extracellular-matrix components. The resulting fibrosis increases intrahepatic vascular resistance and contributes to portal hypertension. The

thesis appropriately highlights the importance of stellate-cell activation and identifies inflammatory and fibrotic pathways as targets for emerging gene and drug therapies [4].

The gut–liver axis is an additional mechanistic layer. Cirrhosis is associated with intestinal dysbiosis and impaired barrier integrity, which can increase translocation of microbial products and stimulate hepatic innate immune responses. The thesis discusses microbiome alterations, Toll-like receptor signaling and the relationship between dysbiosis, oxidative stress and fibrosis [5]. These observations provide a rationale for microbiome-directed therapies, although evidence is not yet sufficient to make most microbiome interventions routine disease-modifying therapy.

Clinical Staging and Natural History

A clinically useful distinction is between compensated and decompensated cirrhosis. Compensated disease may be asymptomatic or associated with subtle fatigue, nutritional impairment or laboratory abnormalities. Decompensation is classically signaled by ascites, hepatic encephalopathy or portal-hypertensive bleeding. AASLD notes that these events represent a major landmark in the natural history of cirrhosis; development of ascites is associated with a marked deterioration in prognosis.

Portal hypertension is a key driver of decompensation. Clinically significant portal hypertension (CSPH) has traditionally been defined using hepatic venous pressure gradient (HVPG), while modern practice increasingly uses non-invasive liver and spleen stiffness measurements to identify patients at clinically meaningful risk. Baveno VIII, published in 2026, confirms the central role of CSPH, expands the use of non-invasive tests, revises cutoffs and emphasizes prevention of first and further decompensation [6].

Prognostic assessment integrates clinical findings and laboratory variables. Child–Pugh classification remains useful for broad severity assessment, while MELD-based scores are central to transplant prioritization. Frailty, sarcopenia, renal dysfunction, hyponatremia and recurrent decompensation provide additional prognostic information and should be considered in multidisciplinary decision-making.

Diagnosis and Non-Invasive Risk Stratification

The thesis describes conventional evaluation using clinical examination, liver function tests, ultrasound, CT, MRI, transient elastography and, in selected cases, biopsy. It correctly emphasizes that transient elastography provides a non-invasive assessment of liver stiffness and that biopsy remains useful when

etiology or histology cannot be adequately defined by non-invasive approaches [7].

Modern diagnosis increasingly begins with non-invasive tests (NITs). Routine laboratory indices—including platelet count, aminotransferases, bilirubin, albumin, international normalized ratio and renal function—are combined with validated fibrosis scores such as FIB-4 and other serum-based algorithms. Vibration-controlled transient elastography and spleen-stiffness measurement can then refine the probability of advanced fibrosis and CSPH. Baveno VIII confirms the expanding role of NITs in compensated advanced chronic liver disease and risk stratification [8].

Ultrasonography remains fundamental for assessment of liver morphology, portal-systemic collaterals, splenomegaly and ascites, and for HCC surveillance. Contrast-enhanced CT or MRI are used when lesions require characterization or when complications need detailed anatomic assessment. Endoscopy remains important for patients who require direct assessment or treatment of gastroesophageal varices. Liver biopsy is now more selectively used, particularly when diagnosis, disease etiology or competing pathologies remain uncertain.

The thesis highlights FibroScan and acoustic radiation force impulse imaging and notes their value for longitudinal monitoring, while also acknowledging limitations in distinguishing every stage of fibrosis [9]. Contemporary practice therefore uses NITs as complementary rather than isolated tests, with interpretation based on disease etiology, inflammation, obesity, cholestasis and clinical context.

Etiology-Specific Disease Modification

Alcohol-Associated Liver Disease

Complete alcohol abstinence is a cornerstone of management. Treatment should include assessment and management of alcohol-use disorder, nutritional rehabilitation, thiamine when indicated, psychosocial support and management of alcohol-associated hepatitis where appropriate. Abstinence can reduce ongoing injury and improve transplant candidacy and long-term outcomes.

Viral Hepatitis

The thesis identifies chronic HBV and HCV as major causes of cirrhosis and emphasizes antiviral therapy [10]. Modern direct-acting antiviral regimens can cure HCV in most treated patients, while nucleos(t)ide analogue therapy suppresses HBV replication and reduces the risk of progression. WHO's current data nevertheless show that access to HBV and HCV treatment remains inadequate globally, making case-

finding, vaccination, linkage to care and affordable medicines essential public-health interventions.

MASLD/MASH

Metabolic dysfunction-associated steatotic liver disease is an increasingly important pathway to advanced fibrosis and cirrhosis. Weight management, physical activity, diabetes control, cardiovascular risk reduction and avoidance of harmful alcohol exposure remain foundational. Newer pharmacotherapy has changed the pre-cirrhotic MASH landscape. Resmetirom was approved in 2024 for adults with non-cirrhotic MASH and moderate-to-advanced fibrosis (F2–F3), and semaglutide received FDA approval for MASH with moderate-to-advanced fibrosis in 2025. These approvals are important advances but should not be described as established treatments for decompensated cirrhosis [11].

AASLD's 2025 update provides practical guidance for selecting and monitoring semaglutide in MASH with F2–F3 fibrosis, reinforcing that these therapies belong to the non-cirrhotic disease-modifying setting rather than being interchangeable with treatment of established decompensated cirrhosis [12].

Autoimmune, Cholestatic and Inherited Disease

Autoimmune hepatitis requires immunosuppression tailored to disease severity and response. Primary biliary cholangitis and other cholestatic disorders require disease-specific therapy and surveillance. Wilson disease, hereditary hemochromatosis and alpha-1 antitrypsin deficiency require targeted diagnostic and therapeutic strategies. The thesis notes that treating the underlying cause can slow progression and, in selected etiologies, permit partial regression of fibrosis [13].

Management of Portal Hypertension and Decompensation

Prevention of First Decompensation

The contemporary goal is increasingly to identify CSPH before ascites or bleeding occurs. Baveno VIII emphasizes non-invasive risk stratification and prevention of decompensation, building on Baveno VII's pathophysiology-based framework [14]. Non-selective beta-blockers (NSBBs), particularly carvedilol in appropriate patients, are central to portal-pressure reduction and prevention strategies. Their use requires attention to blood pressure, renal function and the presence of advanced circulatory dysfunction.

Variceal Bleeding

Acute variceal hemorrhage is a medical emergency. Contemporary care combines early vasoactive therapy,

antibiotic prophylaxis, urgent endoscopic therapy and careful hemodynamic management. Endoscopic variceal ligation is standard for esophageal varices, while early or pre-emptive TIPS is considered in selected high-risk patients. The 2025 EASL TIPS guideline reflects substantial advances in patient selection, prognostic modeling and technical approaches [15].

Ascites and Spontaneous Bacterial Peritonitis

Management includes dietary sodium restriction, appropriately dosed diuretics and therapeutic paracentesis for tense or refractory ascites. Albumin is used in defined clinical situations, especially after large-volume paracentesis and selected circulatory/renal complications. A 2025 AGA expert review emphasizes sodium restriction, the lowest effective diuretic dose, renal/electrolyte monitoring and early diagnostic paracentesis for new-onset ascites or relevant hospital admissions. Refractory ascites should prompt transplant evaluation and consideration of TIPS in suitable patients [16].

Hepatic Encephalopathy

Hepatic encephalopathy reflects a complex interaction of ammonia handling, neuroinflammation, altered astrocyte function, gut microbiota and systemic precipitants. Lactulose remains the principal treatment for overt episodes, while rifaximin reduces recurrence in appropriate patients. The thesis highlights rifaximin

and lactulose as major advances in complication control [17]. Contemporary management also requires systematic identification and treatment of precipitants such as infection, gastrointestinal bleeding, constipation, dehydration, renal dysfunction and sedative exposure.

Hepatorenal Syndrome and Acute Kidney Injury

Renal dysfunction markedly worsens prognosis. Management depends on early recognition, withdrawal of precipitating drugs, volume assessment and treatment of infection or bleeding. Vasoconstrictor therapy with albumin is used for hepatorenal syndrome-acute kidney injury in appropriate settings, and terlipressin has an increasingly defined role in evidence-based protocols. The thesis cites contemporary practice guidance on terlipressin for cirrhosis-related complications [18].

HCC Surveillance

Patients with cirrhosis require regular HCC surveillance according to guideline-based risk. Ultrasound-based surveillance, with or without serum biomarkers according to the clinical setting and guideline, remains central. Suspicious lesions require multiphasic imaging and multidisciplinary assessment. Prevention and treatment of the underlying liver disease remain the most fundamental means of reducing HCC burden.

Table 1: Contemporary Stage-Based Management of Cirrhosis

Disease state	Major priorities	Representative interventions
At-risk chronic liver disease	Prevent fibrosis and identify advanced disease	Vaccination; metabolic control; alcohol avoidance; HBV/HCV testing and treatment; FIB-4/NITs
Compensated cirrhosis	Prevent first decompensation; detect CSPH and HCC	Etiology-specific therapy; NITs; NSBBs when indicated; nutrition; HCC surveillance
Decompensated cirrhosis	Treat complications and prevent recurrence	Ascites therapy; lactulose/rifaximin; variceal prevention/therapy; infection management; renal protection
Refractory/advanced disease	Bridge to definitive therapy	TIPS in selected patients; artificial liver support in selected settings; transplant evaluation
End-stage liver disease	Replace failed organ	Deceased- or living-donor liver transplantation; individualized peri-transplant care

Major Recent Advances

Non-Invasive Portal-Hypertension Assessment

The major conceptual advance is the movement from biopsy-centered diagnosis toward repeated, non-invasive assessment of liver and spleen stiffness, platelet count and clinical features. Baveno VIII confirms that NITs can identify clinically important risk and support earlier preventive intervention [19]. This approach is particularly valuable because fibrosis and portal hypertension are dynamic and may improve after successful treatment of the underlying cause.

Refined Use of Tips

TIPS creates a low-resistance portosystemic channel to reduce portal pressure. Its use has evolved from rescue therapy toward carefully selected early or pre-emptive intervention for high-risk variceal bleeding and selected refractory ascites. The 2025 EASL guideline specifically addresses patient selection, prognostic modeling, indications and technical considerations [20].

Artificial and Extracorporeal Liver Support

The thesis discusses albumin-based extracorporeal systems such as the Molecular Adsorbent Recirculating System (MARS), Prometheus and single-pass albumin dialysis as bridge therapies in severe liver dysfunction [21]. These technologies can remove selected toxins and support physiologic stability, but they do not replace the full synthetic and regenerative functions of a liver and have not displaced transplantation as definitive therapy.

Microbiome-Directed Therapy

The gut microbiome is increasingly viewed as a modifiable component of cirrhosis biology. Approaches under investigation include rational probiotics, defined microbial consortia, antibiotics, dietary interventions and fecal microbiota transplantation. The principal challenge is heterogeneity: microbial signatures differ with geography, diet, medication exposure, disease etiology and severity. Therefore, microbiome therapy should currently be considered an emerging research area rather than a universal standard of care.

Antifibrotic and Disease-Modifying Strategies

The thesis discusses obeticholic acid, cenicriviroc, selonsertib and other pathway-directed agents. Importantly, several historically promising candidates have failed to demonstrate adequate clinical benefit in advanced trials, illustrating that reducing a single molecular pathway may not be sufficient to reverse established cirrhosis. The field is moving toward

combination approaches targeting inflammation, stellate-cell activation, extracellular-matrix turnover, metabolic dysfunction and tissue repair.

Resmetirom and semaglutide illustrate an important distinction: modern disease-modifying therapy has achieved regulatory success in non-cirrhotic MASH with F2–F3 fibrosis, but these agents should not be presented as established antifibrotic treatments for decompensated cirrhosis [22].

Regenerative Medicine, Stem Cells and Organoids

Stem-cell approaches aim to provide anti-inflammatory, immunomodulatory and regenerative effects rather than simply replacing hepatocytes. Recent reviews report a growing clinical-trial landscape, especially for mesenchymal stromal cells, while also emphasizing inconsistent protocols and unresolved safety and efficacy questions [23]. A 2026 GRADE-based systematic review found very-low-certainty evidence for mortality benefit despite signals for improved MELD scores, underscoring the need for high-quality randomized trials before routine clinical adoption [24].

Organoids and extracellular-vesicle platforms provide complementary opportunities for disease modeling, drug screening and potentially cell-free regeneration. These approaches remain experimental and should be clearly separated from established transplantation and supportive therapies.

Gene Therapy and Tissue Engineering

The thesis proposes gene therapy and tissue engineering as future strategies directed at stellate-cell activation, inflammation, regeneration and extracellular-matrix remodeling [25]. In practice, these approaches remain investigational. Major barriers include delivery to the correct hepatic cell population, durability of gene modulation, off-target effects, tumorigenicity, manufacturing complexity and the need to demonstrate clinically meaningful outcomes.

Artificial Intelligence and Precision Medicine

AI is being investigated for image interpretation, fibrosis and cirrhosis prediction, HCC detection, prognostication, transplant outcome prediction and treatment-response modeling. The thesis proposes integration of laboratory data, imaging, genetic information and clinical history to individualize therapy [26]. Recent reviews similarly identify AI, liquid biopsy, extracellular vesicles and non-coding RNA biomarkers as components of a potential precision-hepatology ecosystem [27]. Clinical implementation nevertheless requires external validation, explainability, protection against dataset

bias and demonstration of improved patient outcomes rather than diagnostic accuracy alone.

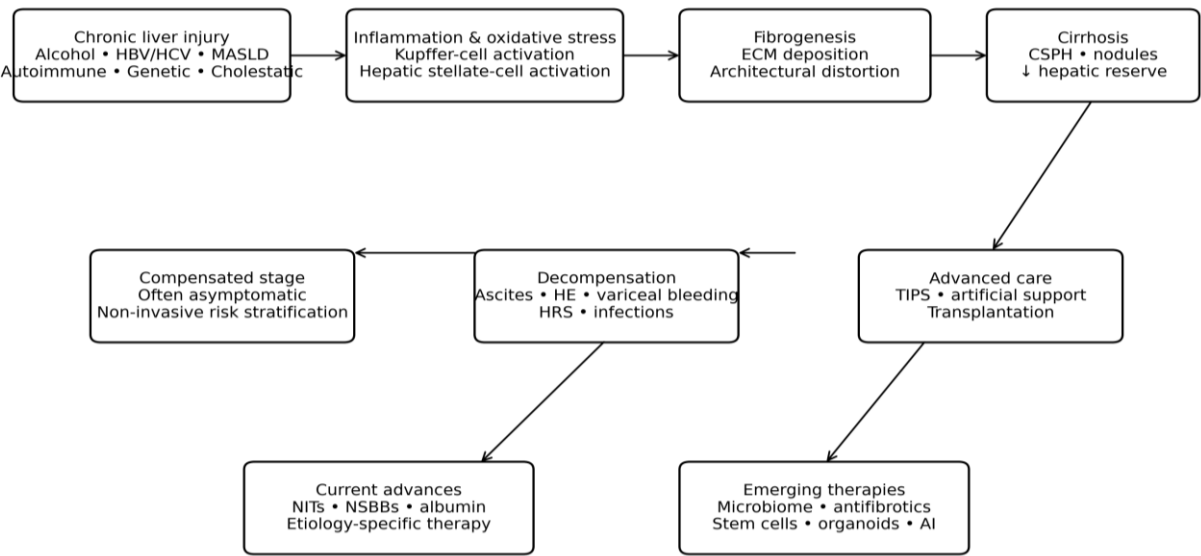


Figure 1: Pathobiology-to-management framework showing progression from chronic liver injury through fibrosis, cirrhosis and decompensation, and the integration of established and emerging therapeutic approaches.

Table 2: Established vs Emerging Approaches.

Approach	Current position	Key opportunity	Main limitation
Transient/spleen elastography	Established	Repeatable non-invasive risk stratification	Cutoffs vary with etiology and context
NSBBs/carvedilol	Established in selected CSPH	Prevention of decompensation and bleeding	Hypotension/renal dysfunction limit use
TIPS	Established, increasingly refined	Control of refractory portal-hypertension complications	HE, cardiac dysfunction and procedural risk
Albumin-based support	Established in defined indications	Circulatory/renal support	Cost and context-dependent benefit
Rifaximin/lactulose	Established for HE	Reduce recurrence and improve HE control	Does not correct underlying cirrhosis
Resmetirom/semaglutide	Established for selected non-cirrhotic MASH	Disease modification before cirrhosis	Not established for decompensated cirrhosis
Microbiome therapy	Emerging	Target gut–liver axis	Heterogeneous evidence and protocols
Stem cells/exosomes/organoids	Investigational	Regeneration and antifibrotic effects	Low-certainty clinical evidence
AI/precision medicine	Emerging	Risk prediction and individualized care	Bias, explainability and external validation
Gene therapy/tissue engineering	Experimental	Potential structural repair	Delivery, safety and manufacturing barriers

Nutrition, Frailty and Patient-Centered Care

Malnutrition and sarcopenia are common and clinically important in cirrhosis. Management should avoid prolonged fasting, provide adequate energy and protein, and tailor sodium restriction to the presence and severity of fluid retention. Exercise and resistance training can support muscle function when clinically appropriate. The thesis emphasizes nutritional support and the importance of lifestyle modification, particularly for metabolic and alcohol-associated disease [28].

Patient-centered care should also address medication safety. Cirrhosis changes drug pharmacokinetics and pharmacodynamics, and nephrotoxic, sedating or hemodynamically active medicines may become hazardous. Medication reconciliation, avoidance of unnecessary non-steroidal anti-inflammatory drugs, careful diuretic titration and individualized analgesia are important components of pharmaceutical care.

Vaccination, infection prevention, early recognition of decompensation, psychosocial support, alcohol-cessation services and advance-care planning should be integrated into long-term management. The pharmacist has an important role in medication review, adherence, drug-interaction screening, patient education and monitoring for adverse effects.

Liver Transplantation

Liver transplantation remains the definitive treatment for appropriately selected patients with end-stage liver disease and selected complications of cirrhosis. The thesis emphasizes advances in surgical technique, donor selection, immunosuppression and post-transplant care, as well as the contribution of living-donor transplantation to the organ shortage problem [29].

Contemporary transplant evaluation should be triggered by clinically significant decompensation, refractory complications, HCC meeting transplant criteria, or progressive liver failure rather than waiting for catastrophic deterioration. MELD-based prioritization is supplemented by clinical judgment and disease-specific exception pathways. Frailty, sarcopenia, cardiopulmonary status, infection risk and psychosocial factors are increasingly incorporated into candidate assessment.

Transplantation has also become more personalized. Living-donor transplantation can reduce waiting time in selected settings, while advances in organ preservation, machine perfusion and donor-recipient matching are expanding the usable donor pool. Nevertheless, donor safety, immunologic

complications, infection, malignancy and lifelong follow-up remain important considerations.

Research Gaps and Future Directions

Develop validated, etiology-aware NIT algorithms that predict decompensation rather than fibrosis alone.

Define combination disease-modifying regimens capable of targeting inflammation, stellate-cell activation, extracellular-matrix remodeling and metabolic dysfunction simultaneously.

Standardize microbiome-based interventions and identify which microbial changes are causal rather than simply associated with disease severity.

Establish the clinical efficacy, safety and optimal cell source/dose for stem-cell and extracellular-vesicle therapies through adequately powered randomized trials.

Improve AI model transparency, calibration and external validation across diverse populations and healthcare systems.

Integrate digital biomarkers, imaging, circulating biomarkers and clinical scores into dynamic models that can be updated during longitudinal care.

Expand equitable access to HBV vaccination, HBV suppression and curative HCV therapy, especially in low- and middle-income countries.

Improve transplant access through living donation, organ preservation, machine perfusion and fair allocation systems.

Conclusion

Management of liver cirrhosis has moved from a predominantly complication-oriented model toward earlier diagnosis, prevention of decompensation and individualized, etiology-directed care. The thesis correctly identifies the central roles of alcohol, viral hepatitis, metabolic liver disease, autoimmune and inherited disorders, and highlights major advances in non-invasive diagnosis, pharmacological management, portal-hypertension control, artificial liver support, transplantation, regenerative medicine and AI.

The most clinically mature advances are improved non-invasive risk stratification, CSPH-directed management, refined TIPS selection, effective antiviral therapy, modern management of ascites and hepatic encephalopathy, and increasingly sophisticated transplantation. Baveno VIII in 2026 further strengthens the emphasis on NIT-based risk assessment and prevention of decompensation. Meanwhile, stem cells, organoids, microbiome therapy, antifibrotic combinations, gene therapy and

AI represent an important research frontier but should not be overstated as established treatments. The future of cirrhosis care is likely to combine early molecular and non-invasive detection with etiology-specific disease modification, dynamic risk prediction, multidisciplinary complication management and timely transplantation.

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Conflict of Interest

None declared.

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