Indian National Association for the Study of Liver (INASL) Guidance Statements for Determining Futility in Liver Transplantation

Anil Arora [*], Praveen Sharma [*], Ashish Kumar [*], S. K. Acharya [†], Shiv K. Sarin [‡], Ajay Duseja [§], Pankaj Puri [¦], Samir Shah [¶], Y. K. Chawla [†], P. N. Rao [#], Anoop Saraya [**], Ravi Mohanka [††], Shweta Singh [‡‡], Sanjeev Saighal [‡‡], Mohamed Rela [§§], Vivek Vij [¦¦], Sonal Asthana [¶¶], Akash Shukla [##,***], Prashant Bhangui [†††], Neeraj Saraf [†††], Rakhi Maiwall [‡], Amit Mandot [¶], Vivek Saraswat [§], Kaushal Madan [‡‡], Shalimar [**], Dharmesh Kapoor [‡‡‡,§§§], Anil C. Anand [†], Subhash Gupta [‡‡], Joy Varghese [¦¦¦], Naimish Mehta [*]

[*] *Institute of Liver Gastroenterology & Pancreatico Biliary Sciences. Sir Ganga Ram Hospital, Rajinder Nagar, New Delhi, 110060, India,* [†] *Kalinga Institute of Medical Sciences (KIMS), Kushabhadra Campus (KIIT Campus-5), Patia, Bhubaneswar, 751024, Odisha, India,* [‡] *Institute of Liver and Biliary Sciences, Delhi, India,* [¶] *Institute of Liver Disease, HPB Surgery and Transplant, Global Hospitals, Dr E Borges Road, Parel, Mumbai, 400012, India,* [#] *Asian Institute of Gsstroenterology, Hyderabad, India,* [**] *All India Institute of Medical Sciences, New Delhi, India,* [##] *Reliance Foundation Hospital and Research Centre, Mumbai, India,* [‡‡] *Max Hospital Saket, Delhi, India,* [§§] *Dr. Rela Institute & Medical Centre, #7, CLC Works Road, Chromepet, Chennai, 600044, India,* [¦¦] *Fortis Hospital, Noida, Delhi, India,* [¶¶] *Aster CMI Bangalore, Aster RV Bangalore, Aster Whitefield, Bangalore, India,* [***] *Seth GSMC & KEM Hospital, Mumbai, 400022, India,* [†††] *Medanta Hospital, Gurugram, Haryana, India,* [¦] *Fortis Excorts Hosiptal, New Delhi, India,* [§] *Post Institute of Medical Sciences, Chandigarh, India,* [‡‡‡] *Mahatma Gandhi Medical College and Hospital, RIICO Institutional Area, Sitapura, Tonk Road, Jaipur, 302022, Rajasthan, India,* [§§§] *Yashoda Hospital, Hyderabad, India,* [¦¦¦] *Gleneagles Global Health City, 439, Cheran Nagar, Perumbakkam, Chennai, Tamil Nadu, 600100, India and* [††] *Sir HN Reliance Foundation Hospital, Mumbai, India*

Liver transplantation (LT) is a life-saving procedure for patients with end-stage liver disease; however, with the growing shortage of organ donors, the need to identify futile transplants has become increasingly urgent. Futility in LT refers to situations where the expected post-transplant survival or quality of life is poor, making the procedure unlikely to yield a meaningful benefit. Various definitions of futility are used across different countries and transplant centers, with criteria often based on clinical factors such as age, comorbidities, Model for End-Stage Liver Disease score, and functional status. For hepatologists and transplant surgeons, clearer guidelines are essential to make informed decisions and avoid unnecessary transplants that may place patients at risk without improving their prognosis. While some studies have proposed futility scores, there is currently no universal consensus on a standardized definition or set of criteria. This highlights the need for further prospective trials to evaluate the predictors of futility in LT, aiming to refine decision-making processes, optimize organ allocation, and improve patient outcomes. Future research should focus on the development of universally accepted futility criteria and explore interventions to mitigate the factors contributing to transplant futility. (J Clin Exp Hepatol 2025;15:102539)

Liver Transplantation

Futility in transplantation is an emerging concept based on utility and beneficence, with varying interpretations across countries and centers due to differences in expertise, cost, and donor availability. Even minimal chances of survival for critically ill patients are not considered futile if they face imminent death without a transplant. However, poor post-transplant survival compared to healthier patients can compromise beneficence when donor organs are scarce.

The method involved in formulating the statements: It was a planned single-theme meeting organized by the Indian National Association for the Study of the Liver (INASL) on June 4th and 5th, 2022, in New Delhi, involving Hepatologists and liver transplantation (LT) surgeons who deliberated extensively on the topic. These discussions led to the drafting of comprehensive guidance statements aimed at establishing clear criteria for identifying futile LT scenarios. The questions were meticulously framed by members of the INASL, all of whom are experts in their respective fields. A detailed literature search was conducted to ensure the inclusion of comprehensive and relevant information. The process involved several Zoom meetings where the statements were discussed and finalized. Following this, a physical meeting was held to conduct the voting process.

Received: 22.5.2024; *Accepted:* 24.2.2025; *Available online 28 March 2025*
Address correspondence: Anil Arora, Department of Gastroenterology, Sir Ganga Ram Hospital, New Delhi, India.
E-mail: Dranilarora50@gmail.com
Abbreviations: ACLF: acute on chronic liver failure; ALF: acute liver failure; APASL: Asian pacific association for the study of liver; DDLT: diseased donor liver transplantation; LT: Liver transplantation; PoPH: Porto pulmonary hypertension; HCC: Hepatocellular carcinoma; MELD: Model for End-Stage Liver Disease
https://doi.org/10.1016/j.jceh.2025.102539

Table 1 Level of Evidence and Grade of Recommendations (Adapted From Grading of Recommendations, Assessment, Development and Evaluations [GRADE] System With Minor Modifications[a])[1,2].

Level of evidence[b]		**Confidence in the evidence**
High	Information obtained from meta-analyses or systematic reviews, or from numerous randomized trials that have high quality data.	It is improbable that additional research will significantly alter our level of confidence in the assessment of potential benefits and risks.
Moderate	Information obtained from either a singular randomized controlled trial (RCT) or various non-randomized studies.	Additional research, if conducted, may potentially alter our estimation of the benefit and risk and have an impact on our level of confidence in the estimate.
Low	Studies of limited sample size, observational studies conducted retrospectively, and registries.	There is a degree of uncertainty associated with any estimate of the effect.
Recommendations – Grade[c]		**Wording associated with the grade of recommendation**
Strong	The strength of the recommendation was influenced by several factors, such as the quality of the evidence, the presumed outcomes that are important for the patient, and the cost implications.	"Must", "should", or "we recommend"
Weak	The recommendation may be made with less certainty and may result in higher costs or resource consumption due to variability in preferences and values, or increased uncertainty.	"can", "may", or "we suggest"

[a]To make the GRADE system more objective, the type of studies from which the evidences are derived have been mentioned in the Level of Evidence section.
[b]Level was graded down if there was a poor quality, strong bias or inconsistence between studies; level was graded up if there was a large effect size.
[c]Recommendations reached by consensus of the members and included the quality of evidence, presumed patient-important outcomes and costs.

Statements were only included in the final document if they received more than 80% agreement from the members and recommended as per Table 1 guidelines.

Concept of futility

LT is the only long-term definitive therapy for patients with liver diseases with decompensation and acute and acute-on-chronic liver failure fulfilling established criteria. These patients generally have good outcomes without comorbid conditions and other organ failures. However, some patients are very sick, with or without extrahepatic organ failure and frailty.[3] Such patients have high mortality without transplant, and if transplanted, overall survival (OS) is compromised compared to those without comorbid conditions, extrahepatic organ failure, and low Model for End-Stage Liver Disease (MELD) scores. The decision to proceed with LT in these cases is difficult due to the lack of clear guidelines and the shortage of donors.[4,5]

Currently, there are no definitive guidelines on post-transplant survival duration, which varies by center, country, and transplant program (living or cadaveric donor). The principle of utility in centers with Living donor liver transplantation (LDLT) programme focuses on maximizing benefits for both the donor and the recipient. It involves a thorough evaluation to ensure that the donor's health is not unduly compromised and that the recipient will gain significant improvements in quality of life and survival prospects.[6] The benefits of LDLT include reduced waiting times and timely transplantation, which can prevent deterioration in the recipient's condition. LDLT has advanced rapidly in Asia, demonstrating good outcomes for both donors and recipients. However, LDLT remains a complex and demanding procedure with significant ethical dilemmas, particularly regarding the risks to the donor. The transplant team must be well-versed in bioethics to address these concerns. The principles of autonomy, beneficence, and non-maleficence should guide decisions, ensuring the donor's safety while optimizing recipient outcomes. According to the concept of equipoise, the potential risk to the donor must be balanced with the expected benefit to the recipient.[7] The cost of the procedure is a major consideration, especially in developing countries where LDLT is predominant. Cadaveric transplants face similar issues but with less concern for the donor.

Meaningful benefits after transplant are considered with parameters such as post-transplant 3-month survival, one-year or five-year survival of more than 50%, and in-hospital mortality of less than 50%, based on country or center-specific ethical standards. The concept of futility in LT is complex, as LT remains the only hope for survival for patients with high short-term mortality without it.[8,9] Ethical clinical practice varies with cultural and geographical views, resource availability, and who bears the cost of LT. These views influence the decision to deny or delay LT in critically ill patients, impacting OS rates.[10]

Ethical consideration for defining futility

In clinical practice, medical decision-making in LT is guided by five ethical principles: autonomy, beneficence, non-maleficence, justice, and utility. Utility aims to maximize community benefit by balancing good and minimizing harm, a challenge in LT due to limited donor organs and resources. There are no universal guidelines for determining beneficial LT outcomes, which may include short-term survival (3–6 months) or 1, 3, and 5-year survival rates above 50%. Other factors include complications, quality of life, and the effects of immunosuppressive medications. The utility of LT depends on donor availability, funding, and the transplant type (donor liver transplantation [DDLT] vs. LDLT).[8–10] Defining futility in LT is complex, as it must align with these ethical principles. While utility favors better outcomes for less sick patients, justice prioritizes the sickest patients, even with poorer survival prospects. This results in a delicate balance when considering futility, with no universally accepted definition. Futility is an evolving concept that remains without a universally accepted definition despite extensive expert discourse. The complexity and variability inherent in medical situations contribute to the lack of consensus.[11] There was a discussion on contraindication in LT and how it differs from futility in LT. It was decided that all contraindications should be considered futile in LT at that point of time, but not all futility transplants are contraindications, as they vary from patient to patient, center to center, and society to society in different countries, depending upon the availability of donors, funds, and type of LT program (DDLT versus LDLT).

Definition of futility (opinions of a hepatologist, surgeon, and intensivist)

There was a long debate among participants on what should constitute futility in LT. It was argued that futility should be defined within the context of evolving standards of care and that the goal of LT is to achieve a benefit above a certain minimum qualitative or quantitative threshold. The concept of futility may be considered in LT under three conditions: when LT cannot fulfill its physiological role in reversing disease (physiological futility), when the success rate of the transplant is less than 1% (quantitative futility), or when LT cannot ensure an acceptable quality of life after the procedure (qualitative futility).

Most LT societies and professionals would offer LT if the expected 5-year survival rate is more than 50–60%, although there is a lack of consistency in the outcomes measured (mortality, graft function, etc.) and timelines (1, 3, and 6 months or 1, 3, and 5 years). We should strive to achieve the balance stated in the National Organ Transplant Act (USA) and published in the OPTN Final Rule: "We must strive for a system that minimizes waitlist mortality while avoiding futility of transplantation." The decision to transplant should be based on the patient's sickness and its expected responsiveness to the transplant. Unfortunately, futility is often known only in retrospect.[12] Our goal is to predict and avoid such transplants.

The futility of LT could be due to donor or recipient factors. Therefore, instead of using the word "futile," we could risk-stratify transplants as standard risk, high risk, and contraindication.

Need for LT and waitlist mortality in India

India faces a significant and growing burden of LT due to the rising prevalence of chronic liver diseases, including viral hepatitis, alcohol-related liver disease, and metabolic syndrome associated steatotic liver disease. Despite the increasing need, organ availability remains critically low, with a donor rate of approximately 0.8 per million population. This severe organ shortage has led to alarmingly high waitlist mortality rates. Recent studies report waitlist mortality as high as 44.19% during 2019–2021, exacerbated by the COVID-19 pandemic.[13] Another study documented a one-year waitlist mortality rate of 27.7%.[14] Limited access to LT centers and delayed organ allocation contribute to these fatalities. Public awareness campaigns, better donor management systems, and enhanced cadaveric donation programs are urgently needed to mitigate this crisis. Improving policy frameworks and healthcare infrastructure can significantly reduce mortality and address the unmet demand for LT in India.

Futility of LT in acute liver failure

LT is often the only chance of survival for patients with acute liver failure (ALF) who meet transplant criteria. However, accurately predicting outcomes in ALF remains challenging due to the lack of a reliable prognostic model. Major issues with LT in ALF include the timely availability of donors, the rapidly changing condition of patients on the waiting list, unclear delisting criteria at many centers, limited time for pre-transplant evaluation, ethical concerns related to poisoning or suicidal attempts, and relatively lower post-transplant outcomes compared to other indications for LT.

Francesco Figorilli *et al.*[15] defined futile LT as death within 48 h of surgery due to the development of multi-organ failure and/or irreversible brain damage, excluding major surgical complications like HAT, Portal vein thrombosis (PVT), outflow obstruction, hemorrhagic shock, and primary graft non-function. The Acute Liver Failure-Organ Failure score (ALF-OFs) was calculated as (CLIF-C OF x

0.391) + (Norepinephrine mcg/min x 0.020). A score above 6.5 was a significantly better predictor of death compared to existing scores of CLIF-C OF ($P = 0.044$) and King's College Hospital criteria (KCH) ($P < 0.0001$).

Several factors predict poor post-LT survival, including:

1. Obesity (body mass index [BMI] >30 kg/m^2)
2. Age over 50 years
3. Higher MELD scores
4. Incompatible ABO matching
5. Pre-transplant waiting time >5 days
6. Lower pH (≤7.26)[16]

In a study of 84 ICU patients who received LT, including 29 with ALF and 55 with acute-on-chronic liver failure (ACLF), the mean MELD score was 41 and the mean SOFA score was 15 before transplant. The overall 1-year survival rate was 66%. Multivariate analysis identified pretransplant lactate levels and acute respiratory distress syndrome (ARDS) as independent factors associated with post-transplant mortality. Patients without ARDS and with pretransplant lactate levels below 5 mmol/L had a higher than 80% 1-year survival.[17]

All contraindications for LT in patients with ALF are considered futile, as outlined in the INASL ALF statement.[18] The need for robust data on poor predictors of post-LT outcomes was emphasized. Acute hepatic failure which was complicated by toxic liver syndrome is a medical emergency. It requires emergency hepatectomy for stabilization of the patient followed by graft implantation to prevent futility of LT.[19]

Statements on Futile Liver Transplantation in Acute Liver Failure

Statement	Level of evidence	Strength of recommendation
ALF is a dynamic condition and the patient should be monitored regularly and LT should not be done if patient is improving	Low	Weak
Three or more organ failures which include circulatory failure on two inotropic support and limited response on further dose escalation, maximum ventilator support (FiO2>0.8, high PEEP) for respiratory failure, or on ECMO	Moderate	Strong
Active sepsis and invasive fungal infection	Low	Weak
Proven brain death	Moderate	Strong

ALF: acute liver failure.

Futility of LT in ACLF

ACLF is characterized by the development of organ failure and high short-term mortality in patients with known or unknown chronic liver disease. Although its definition varies among societies, the high short-term mortality rate is a common factor. ACLF is classified into various grades based on the number of organ failures, with mortality increasing as the number of organ failures rises.[20–22]

1. **Screening and Listing for LT**:
   - All ACLF grade 1 and 2 patients should be screened and listed for LT.
   - LT for ACLF-3 patients is debated due to high associated mortality, with some studies showing good outcomes while others indicate very poor results for the sickest patients.[23–26]
2. **Factors Influencing LT in ACLF Patients**:
   - Grade of ACLF
   - Availability of donors
   - Timing of LT in ACLF
   - Quality of the donor liver
   - Age of the donor and associated comorbidities as assessed by various scores like University of California Los Angeles-Futility Risk Score, age-adjusted Charlson comorbidity index, and CLIF-C ACLF score
   - Potential for recovery through medical management

ACLF patients exhibit a dynamic disease course similar to ALF, making LT challenging due to factors like timing and donor and patient selection. The principles of LT should align with utility and beneficence, specific to each country. Positive outcomes can be achieved by:

- Early mobilization to specialized centers
- Identifying opportunistic windows for LT early in the disease course
- Intensive treatment for early organ failures
- Timely donor identification and patient selection

More evidence from prospective studies on sicker ACLF patients is needed to guide LT decisions. Currently, LT in ACLF-3 should be considered a relative contraindication, not futile, as ACLF does not negatively impact post-transplant survival or long-term complications.[27,28] The balance between hospital resources and patient outcomes in ACLF-3 remains a matter of debate. Sicker patients require extended hospital stays and resources. In a retrospective multicenter study, Artzner *et al.*[27] identified four factors independently associated with post-transplant mortality: age over 53 years, pre-transplant arterial lactate >4 mmol/L, mechanical ventilation with a PaO2/FiO2 ratio <200, and pre-transplant leukocyte count <10 G/L. They developed the Transplantation for ACLF-3 Model (TAM), where each risk factor contributed 1 point to the score. A TAM score >2 was linked to a significantly reduced

1-year survival rate, with rates of only 8.3% in the initial cohort and 10% in a validation cohort.[27] Additionally, a study from 10 North American centers found that PVT in ACLF-3 patients was associated with a substantial reduction in 1-year post-transplant survival (57% vs. 92%).[29] Recently multicenter study by Artru *et al.*[30] included ACLF-3 (n = 73) and compared it with matched controls patients with ACLF-2 (n = 145), 1 (n = 119) and no ACLF (n = 292). All ACLF-3 patients had a median follow-up of 7.5 years and concluded that five-year survival rates were similar across all groups (about 70–77%), and 10-year survival for ACLF-3 was 56.8%, with no major differences compared to other groups. This study emphasizes that long-term survival after a LT in ACLF-3 is significantly affected by the risk of infections and heart-related issues. It highlights the importance of using health evaluation scores, like the age-adjusted Charlson comorbidity index, to assess a patient′s overall health when considering transplantation and focus on reducing infection risks with personalized treatments and managing heart health after the procedure. Another prospective study which enrolled 200 ACLF patients admitted to ICU and ultimately 50(25%) had LT, highlighted the importance of prolonged mechanical ventilation (respiratory failure>7 days) and the increasing number of organ failures >2 since admission at day 3 as criteria for LT futility.[31]

A national prioritized liver graft allocation program for ACLF was initiated in the UK in May 2021 across seven LT centers. Candidates required cirrhosis, critical care organ support, and >50% predicted 1-month mortality, with exclusions based on age ≥60, prior LT, comorbidities, or substance misuse. Fifty-two patients were registered; 81% received a transplant within 2–5 days, and all non-transplanted patients died within a median of 7 days. Post-transplant survival was 77% at 1 year, demonstrating LT as a highly effective treatment for selected critically ill ACLF patients. This study marks the first prospective national initiative targeting this population[32]

A study of 3636 patients listed with ACLF-3 undergoing LT found that 24.5% recovered to ACLF 0–2, while 75.5% remained at ACLF-3. One-year survival was 82.0% for those with ACLF-3 at transplantation, compared to 88.2% for those improving to ACLF 0–2. Survival was lower for patients who progressed from ACLF 0–2 to ACLF-3 at LT. Cox modeling showed that recovery from ACLF-3 to ACLF 0–2 improved post-transplant survival, especially in those recovering from circulatory or brain failure or those removed from mechanical ventilation. This effect was also seen in patients over 60 years old.[33]

In a multicenter study, the Simplified Mortality Prediction Scores (SMOPS) model was developed using six pre-transplant risk factors(chronic liver failure/organ failure scores, fever >37.6 °C, ABO blood-type compatibility, arterial lactate level, leukocyte count and re-LT) to predict post-liver transplant mortality in 544 patients, with validation in 276 additional patients. SMOPS outperformed MELD and other models in predicting 30-day, 90-day, and 365-day mortality. It stratifies risk into four levels: low risk (<10 points), moderate risk (11–20 points), high risk (21–25 points), and futile risk (≥26 points). Survival outcomes were similar regardless of MELD score or acute versus chronic liver failure. SMOPS offers an improved prediction for the Chinese population and may enhance organ allocation strategies.[34]

Consensus Statements on Futile LT in ACLF

Statement	Level of evidence	Strength of recommendation
LT in patients with ACLF will be considered futile if:		
1. Increasing organ failure>2 from day of admission	Moderate	Strong
2. Sepsis with ≥ 2 organ failure	Moderate	Strong
3. Uncontrolled sepsis after 72 h of antibiotics/antifungal	Moderate	Strong
4. Advanced azotemia, [S. Cr > 4 mg/dl or 3 times increase or renal replacement therapy	Moderate	Strong
5. Respiratory failure [severe ARDS defined by a *PaO2/FiO2 ratio < 150]*	Moderate	Strong
6. Active gastrointestinal bleeding	Moderate	Strong
7. Hemodynamic instability requiring > 1mcg/kg/min or 3 mg/h noradrenaline, lactate >9 mmol/L, lack of resolution after 4–7 days of ICU care	Moderate	Strong

ACLF: acute-on-chronic liver failure; ICU: intensive care unit; LT: liver transplantation.

Futility of LT in hepatocellular carcinoma

LT is the best curative treatment for patients with hepatocellular carcinoma (HCC) and associated liver cirrhosis. The selection for LT was primarily based on the Milan criteria, which yields a 5-year survival rate exceeding 70%.[28] With a better understanding of HCC and identification of surrogate markers of tumor biology, the criteria for LT have expanded beyond just size or number of tumors. New criteria include factors such as alpha-fetoprotein (AFP) levels over 1000 ng/mL, PET scan positivity, and histology.[35] Studies have shown that RETREAT score (microvascular invasion [MVI], AFP at time of LT, and the sum of the largest viable tumor diameter and number of viable tumors on explant) can also predict unfavorable LT and a higher score of >4 may suggest futility.[36–38] Unfavorable tumor characteristics increase the risk of recurrence, impacting post-transplant survival, and raising questions about the point at which LT becomes futile for these patients. A multicenter cohort study (2000–2018) analyzed HCC patients undergoing LT after locoregional therapy (LRT), excluding those with AFP >1000 ng/ml. Of 2441 LT patients, 70.1% had prior LRT; downstaging (DS) was successful in 45.2% of UCSF-DS(University of California, San Francisco down-staging) and 38.2% of all-comers. Recurrence risk was significantly higher in all-comers (SHR 6.01) but not in UCSF-DS patients compared to Milan criteria. AFP ≤20 ng/ml improved outcomes in UCSF-DS, but all-comers had poor survival regardless of AFP. Optimizing LT candidate selection using AFP ≤20 ng/ml may enhance UCSF-DS outcomes.[39] In another study, it compared outcomes of DS to Milan criteria between patients with HCC exceeding UCSF-DS criteria ("all-comers") and those within UCSF-DS. Successful DS was achieved in 64.8% of all-comers versus 84.2% of UCSF-DS patients. The all-comers group had higher dropout rates (53.5% vs. 25.0% at 1 year) and significantly lower LT rates (13.5% vs. 59.0%). Factors predicting dropout included higher tumor burden (size more than 8 cm) and advanced liver disease (Child class B/C). Intent-to-treat survival and post-LT outcomes were worse for all comers, suggesting a tumor burden limit beyond which LT success is unrealistic and futile.[40] The selection criteria for HCC patients differ between DDLT and LDLT, and thus the futility criteria differ as well. Defining futility in DDLT aims to avoid organ wastage and is considered reasonable to set a 5-year survival rate of 50% or more for both cadaveric and living donor LT outcomes. UNOS database analysis (2012–2015) showed that 3-year post-LT survival was highest for Milan criteria (83.2%), followed by UNOS-DS (79.1%) and AC-DS(all-comers) (71.4%). Higher AFP (≥100 ng/mL) and shorter wait time's increased post-LT death and HCC recurrence risk in down-staging groups.[41] Meta-analysis of 25 studies (3997 patients) found a DS success rate of 55.16%, with 31.52% undergoing LT and 16.01% experiencing HCC recurrence. Studies using UNOS-DS criteria showed significantly better DS success (83.21% vs. 45.93%) and lower recurrence (9.06% vs. 20.42%) compared to non-UNOS-DS criteria. ITT 5-year survival post-LT was 74% for UNOS-DS patients, supporting its clinical utility for improved outcomes[42] Predicting tumor recurrence, particularly in LDLT, is challenging and essential to prevent unnecessary surgery risks to the donor. In a study compared outcomes for patients meeting UCSF criteria (n = 159) and UCSF + criteria (largest tumor ≤10 cm, any number of tumors, AFP ≤1000 ng/ml) (n = 58), with median follow-up of 28 months. Five-year OS was similar (71% vs. 69%, P = 0.7), but recurrence risk was higher in UCSF+ (36% vs. 13%, P = 0.1). Excluding AFP >600 ng/ml reduced UCSF + recurrence risk to 27%. Among MVI patients, low-risk groups (good response, AFP ≤100 ng/ml) had superior OS (85%, P = 0.003). Incorporating AFP, DS response, and MVI improves outcomes with LDLT beyond standard criteria.[43] In patients with AFP >600 ng/ml, a preoperative biopsy to rule out poor differentiation should be considered for patient selection.[44] Another study showed that in 77 HCC patients, 14% were within UCSF criteria, showing 5-year overall and recurrence-free survival (OS/RFS) rates of 55% and 46% for those exceeding UCSF. High AFP, younger age, and macrovascular invasion predicted poor outcomes.[45] Understanding risk factors contributing to tumor recurrence beyond the Milan criteria is crucial in balancing the reduction of dropout risk in LDLT against increased HCC recurrence post-LDLT.

As expanded criteria for LT in HCC are utilized, especially in countries where LDLT is predominant, defining futility becomes a significant issue for LT teams. While utility arguments may be less relevant, donor responsibility remains critical, including managing morbidity and mortality associated with LDLT and protecting donors from psychological impacts due to poor LT outcomes.

Consensus Statements on the Futility of Liver Transplantation in HCC

Statement	Level of evidence	Strength of recommendation
It is futile to transplant in the presence of extrahepatic disease or progression on locoregional therapy in patients with HCC	Moderate	Strong
In cases of HCC with macrovascular invasion systemic therapy with or without LRT (locoregional therapy) or best supportive care is preferred over LT in patients HCC and Child-Pugh class A, B or C. Patients with complete response to systemic/LRT can be considered for LT after complete evaluation, only under clinical trials. AFP ≥ 100 ng/mL) after LRT predicts higher risk of recurrence and futility. Availability of organs in DDLT and donor risk in LDLT need to be assessed.	Moderate	Strong
HCC in cirrhotic beyond established criteria should be transplanted following downstaging to within criteria to avoid futility. Availability of organs in DDLT and donor risk in LDLT need to be assessed.	Moderate	Strong

AFP: alpha-fetoprotein; DDLT: diseased donor liver transplantation; HCC: hepatocellular carcinoma; LDLT: live donor liver transplantation; LT: liver transplantation.

Futility of LT in intrahepatic malignancies other than HCC

Both short- and long-term survival rates have improved for liver tumors other than HCC, likely due to advancements in immunosuppression and surgical techniques for LT. However, LT for malignancies other than HCC remains debatable due to limited published literature, expertise, and the high likelihood of recurrence post-transplant.

1. **Cholangiocarcinoma (CCA)**: LT may be viable for patients unsuitable for liver resection due to anatomical or liver condition challenges. The Mayo Clinic protocol has shown long-term, disease-free survival for selected patients and is followed in some centers.[46] Key dropout predictors include:
   - CA 19.9 > 500 U/mL
   - Tumor mass >3 cm
   - MELD >20
   - Proven malignancy by biopsy[47] Progression of disease post-protocol treatment excludes patients from the LT list.
2. **Liver Metastasis (LM)**: LT has been investigated for selected malignancies like metastases from well-differentiated neuroendocrine tumors, particularly when no major surgery other than liver surgery is required. Retrospective studies show LT is beneficial when:
   - Disease is confined to the liver or the primary tumor is removed before LT
   - Ki < 10% with a well-differentiated tumor
   - No major extrahepatic resection is needed
   - Follow-up time exceeds 1–2 years to assess disease behavior post-primary tumor resection[48–50]
3. **Colorectal Cancer Metastasis**: LT for unresectable liver metastases from colorectal cancer remains controversial due to limited data on disease-free survival. A prospective follow-up of 21 LTs identified poor survival predictors:
   - Tumor diameter >5.5 cm
   - Primary cancer surgery within 2 years of LT
   - CEA levels >80 mcg/L
   - Evidence of progressive disease at the time of LT Two or more negative prognostic factors indicate poor outcomes and potential futility.[51] Scores like OSLO (<2) and Fong Clinical Risk Score (FCRS <2) show good sensitivity in predicting survival after LT for colorectal metastasis.[51] Recently a study randomized 94 patients (patients aged 18–65 years, with Eastern Cooperative Oncology Group performance score 0–1, permanently unresectable colorectal liver metastases from resected BRAF-non-mutated colorectal cancer responsive to systemic chemotherapy [≥3 months, ≤3 lines], and no extrahepatic disease) with unresectable colorectal liver metastases to LT plus chemotherapy or chemotherapy alone. The 5-year OS was significantly higher with transplantation plus chemotherapy (56.6%) compared to chemotherapy alone (12.6%). Serious adverse events occurred in 80% of transplant patients and 83% of chemotherapy-only patients. The findings support LT as a viable standard treatment for select patients with liver-only metastases.[52]
4. **Emerging Studies**: Some new studies are enrolling patients based on molecular tests, such as BRAF wild-type tumors with microsatellite stability, though long-term results require further validation.[51,53,54]
5. **Rare Primary Tumors**: Hepatoblastoma and hemangioendothelioma are rare liver tumors for which LT can be the only cure. Due to their rarity and lack of prospective follow-up studies, definitive statements on the futility of these tumors cannot be made.[55]

Futility of LT in pregnancy

Managing ALF during pregnancy requires a multidisciplinary team including intensivists, obstetricians, hepatologists, neonatologists, and transplant experts. LT for

pregnancy-associated HELLP syndrome, acute fatty liver of pregnancy, and acute or ACLF is rare,[56,57] resulting in limited data on indications, contraindications, and outcomes.

Outcomes of LT in these cases should consider short- and long-term survival of the patient, fetus, and graft. Standard King's criteria have not been evaluated or validated for pregnancy-associated liver failure due to the lack of such patients in the original cohort. Given the scarcity of published data, it was decided that futility criteria cannot be extrapolated from available case reports and case series. Therefore, the same criteria used for ALF should be followed until more literature is available on this topic.

Futility of LT in Re-transplantation

The incidence of re-transplantation (re-LT) ranges from 5 to 20%.[58] The 5-year graft survival rate for re-LT is approximately 50–65%, compared to 70% for primary LT.[59,60] Re-LT is challenging to deem futile because it is often the only treatment option after primary graft dysfunction and hepatic artery thrombosis (HAT) that cannot be resolved through surgery or radiological intervention. Late re-LT is necessary for issues such as disease recurrence, graft dysfunction, chronic rejection, and other biliary complications that require repeated interventions or hospital stays. The timing of early re-LT after HAT, primary graft dysfunction, and acute severe rejection is crucial since the development of sepsis and multi-organ failure can render the procedure futile.

Several models predict poor outcomes after re-LT. Rosen *et al.*[61] proposed a model considering recipient age, total bilirubin, creatinine levels, and the time interval to re-OLT. The MELD score correlated with outcomes following re-OLT, with median MELD scores being significantly higher in patients who died within 90 days compared to those who survived (25.9 vs. 20.75, respectively, $P = 0.004$). Various studies have shown the following criteria as risk of poor outcome after re-LT as preoperative serum total bilirubin (>13 mg/dL), creatinine (>2 mg dl), MELD >25 (severe decompensation), recipient age (>60 years), UNOS status (ICU, hospital ward, ambulatory), preoperative infection/sepsis (especially MDR), urgent or early (up to 2 months) vs. late re-LT (especially beyond a year), mechanical ventilator support, interval to re-LT, HCV status, donor age (>60), warm (>75 min) and cold ischemia (>12 h) times, extended criteria donors (DCD), adult re-LT vs. pediatric re transplantation.[61–64]

Zimmerman *et al.*[65] concluded that re-LT should be performed within 7 days of early graft dysfunction, as delayed re-LT leads to poorer outcomes. Late re-transplantation shows poor results in patients with MELD >25, those requiring renal and ventilator support, and in older patients. It is also associated with worse outcomes when performed with extended or older donors. All participants agreed that improved prognostic models are needed to better predict futility after re-OLT, taking into account the severity of the disease and the quality of the donor organ.

Liver re-LT has poorer outcomes than primary transplants, requiring careful candidate selection. A retrospective study of 111 patients at the Medical University of Innsbruck (2000–2021) identified a five-year graft and patient survival of 64.9% and 67.6%, respectively. The balance of risk (BAR) score (MELD score, donor age, recipient age, cold ischemia time, re-LT, and the need for life support) predicted graft loss, sepsis, and complications, with sepsis as the most significant risk factor. A BAR score ≥18 correlated with less than 50% graft survival at five years, highlighting its utility for guiding clinical decisions in liver retransplantation.[66]

Consensus Statements on Futility in Re-transplantation

Statement	Level of evidence	Strength of recommendation
Re-transplantation beyond the first week in patients with early graft dysfunction may be considered futile.	Low	Weak
Re-transplantation should not be offered to recipients with alcohol relapse/recidivism as the cause of graft failure	Moderate	Strong
Re-transplantation in patients with MELD >25, especially in those with concomitant significant renal dysfunction, requiring mechanical ventilation may be considered futile	Moderate	Strong
Re-transplantation should not be performed in patients with ongoing sepsis or untreated infection (especially with multi-drug resistant organisms) or BAR score ≥18	Moderate	Strong
Indications for re-transplantation may be expanded in children especially those more than 5 years of age.	Low	Weak

BAR: balance of risk; MELD: Model for End-Stage Liver Disease.

Futility of LT in cardiovascular comorbidities

LT candidates are often obese, over 50 years of age, and have features of metabolic syndrome, along with cardiovascular comorbidities. Asymptomatic coronary artery disease (CAD) is present in 25% of LT candidates.[67] It is also

common to find cirrhotic cardiomyopathy, portopulmonary hypertension (PoPH), and some degree of valvular heart disease. Many of these patients are critically ill and may require vasopressors to manage hypotension.

Preoperative evaluation for CAD in LT patients is crucial, as appropriate cardiovascular revascularization can mitigate the negative impact of CAD on post-transplant survival.[67,68] Approximately 30% of LT patients will develop cardiovascular disease (CVD) complications within one year, including acute cardiac ischemia, arrhythmias, pulmonary embolism, stroke, and heart failure.[67–72]

The Cardiovascular Risk in Orthotopic Liver Transplantation (CAR-OLT) score has been developed to assess the risk of intraoperative and immediate postoperative CVD events after LT. This score is an important predictor of mortality and hospitalization due to cardiac events within one year following LT.[73] The American Society for Transplantation Liver and Intestinal, and Thoracic and Critical Care Communities of Practice have published consensus recommendations for diagnosing and managing CVD in patients with cirrhosis prior to LT.[74]

For critically ill patients with severe symptomatic CAD who require early transplantation, treatment options include metal stents (mainly bare stents), coronary artery bypass grafting (CABG) before LT, or combined LT and cardiac surgery in the same procedure. Severely obstructed, non-revascularized multivessel CAD is considered an absolute contraindication for LT.[74,75]

Cirrhotic cardiomyopathy, a complication of cirrhosis, is characterized by a poor heart response to inotropic and chronotropic agents, altered diastolic relaxation, and electrophysiological abnormalities. It is more common in patients with cirrhosis due to alcohol-related liver disease, hepatitis C, amyloidosis, hemochromatosis, and metabolic syndrome-associated steatotic liver disease (MASLD). In 2020, the Cirrhotic Cardiomyopathy Consortium proposed new criteria for diagnosing cirrhotic cardiomyopathy, which includes key markers of diastolic and systolic dysfunction.[50] While many centers do not perform LT if the ejection fraction (EF) is <40%, some specialized centers do not consider an EF <40% as an absolute contraindication for LT.[76]

PoPH is a rare complication of cirrhosis, often suspected based on clinical symptoms and echocardiographic findings such as a dilated right ventricle, significant tricuspid regurgitation, and right ventricular systolic pressure (RVSP) > 40–50 mmHg. Right heart catheterization can accurately measure pulmonary pressures if echocardiography suggests high pulmonary pressure.[77] Unlike portal hypertension due to left heart failure (which has an elevated pulmonary capillary wedge pressure, PCWP), PoPH is characterized by a low PCWP (<15 mmHg). LT in patients with moderate to severe PoPH has poor outcomes and high mortality. LT should be avoided in patients with severe PoPH who do not respond to treatment (MPAP <35 mmHg & PVR <400 dyn s·cm^{-5}).[77,78]

Stenotic valvular heart disease leads to pressure overload and left ventricular hypertrophy, resulting in poor left ventricular compliance. Ischemic events and life-threatening arrhythmias after LT are commonly observed in such patients, leading to poor survival. LT should be performed with caution, or preferably avoided, in cases of severe or critical aortic stenosis unless preoperative intervention, such as valve repair or transcatheter aortic valve replacement, is performed before LT.

While a pre-existing cardiac arrhythmia is not a contraindication for LT, underlying cardiac pathology must be excluded, as it may prevent successful transplantation. Patients with congenital heart disease often have elevated right heart pressures, which can compromise hepatic function. There is limited literature on this issue, and combined heart and LT may be required for select patients (68.70).

Consensus Statements

Statement	Level of evidence	Strength of recommendation
In coronary artery disease, LT should not be considered in obstructive severe multivessel CAD, which has not been revascularized.	Moderate	Strong
In cardiomyopathy and heart failure, LT should be considered as futile in patients with LVEF <40% or severe right heart failure	Moderate	Strong
LT should not be considered in severe PoPH associated with right heart failure and/or not responsive to pulmonary vasodilators (MPAP <35 mm Hg & PVR <400 dyn s.cm -5). POPH with mPAP of 45 to 50 mm Hg or greater is an absolute contraindication to LT and is considered as futile.	Moderate	Strong
LT may be considered as futile in patients with arrhythmias and associated severe heart failure; patients who are hemodynamically unstable; patients with structural, valvular disease, or ischemic heart disease; or those poorly controlled by medical management.	Moderate	Strong
Liver transplantation should be considered as futile and should not be carried out in circulatory failure on two vasopressor supports with limited response.	Moderate	Strong

CAD: coronary artery disease; LT; liver transplantation; POPH: portopulmonary hypertension.

Futility of LT in pulmonary morbidities

Pulmonary complications in LT candidates can significantly impact intraoperative and postoperative outcomes, leading to increased risks, prolonged ICU stays, and the need for pulmonary support. Early detection and management of these complications are crucial to improving survival rates and preventing unnecessary prolonged hospitalizations. Certain pulmonary abnormalities can increase the risk of LT, making it potentially futile in some cases. However, in selected patients, LT may alleviate pulmonary issues, improving their prognosis.[79,80]

Chronic obstructive pulmonary disease (COPD) is prevalent in LT candidates. Around 80% of these patients are not disqualified from listing for LT due to COPD. However, clinically significant COPD, defined as a forced expiratory volume in 1 s/forced vital capacity (FEV1/FVC) ratio of less than 70%, is observed in only 18% of cases. Despite this, the impact of COPD on hospital admissions, ventilator dependence, and other morbidities has not been thoroughly explored, and further studies are needed to assess the full impact of severe COPD on post-transplant recovery. Currently, there are no specific guidelines to classify advanced COPD as an absolute contraindication to LT, and the long-term outcomes of LT in these patients remain uncertain. COPD severity is a critical factor in survival, with 5-year survival rates for cirrhotic patients with severe COPD (FEV1 <50% of the predicted value) ranging from 50 to 70%. In patients with FEV1 <30% of the predicted value, 5-year survival drops to less than 30%. For cirrhotic patients with COPD exacerbations requiring non-invasive ventilation, the 2- and 5-year survival rates are 52% and 26%, respectively, underscoring the negative effect on survival outcomes.[80,81]

Other rare pulmonary diseases, such as idiopathic pulmonary fibrosis (IPF) or interstitial lung disease (ILD), may also co-occur in LT candidates, particularly those with primary biliary cirrhosis, autoimmune hepatitis, and hepatitis C. These conditions reduce lung capacity to varying degrees and can coexist with hepatopulmonary syndrome (HPS) and arterial hypoxemia, further complicating transplant outcomes. In cases where severe pulmonary restriction due to IPF is present, LT may be deemed futile, and decisions should be made on a case-by-case basis. The average 5-year survival without lung transplantation in IPF patients is typically between 20% and 40%. However, the data on other pulmonary conditions, such as nonspecific pulmonary nodules, the coexistence of HPS with COPD, or hepatic hydrothorax, are scarce, and the futility of LT in these situations cannot be definitively assessed. These cases should be carefully reviewed by a multidisciplinary team, including pulmonologists, to determine the viability of LT based on the patient's overall health status and pulmonary function.[82,83]

Consensus Statements: Futility of LT in Pulmonary Morbidities

Statement	Level of evidence	Strength of recommendation
MPAP >50 mmHg, LT is contraindicated and may be considered futile.	Moderate	Strong
LT is contraindicated in moderate/severe ILD	Moderate	Strong
LT contraindicated in very severe COPD (FEV1 % predicted < 30)	Weak	Low

FEV1: forced expiratory volume in 1 s; ILD: interstitial lung disease; LT: liver transplantation.

Futility of LT in renal morbidities

Kidney dysfunction is common in patients with decompensated cirrhosis, with nearly 80% of hospitalized cirrhosis patients experiencing some form of acute kidney injury (AKI) which is defined as a rapid deterioration in kidney function, typically indicated by an increase in serum creatinine of ≥0.3 mg/dL within 48 h or a 50% increase in serum creatinine from baseline. Additionally, AKI is also defined by a urine output of less than 0.5 mL/kg/hour for more than 6 h. Early identification and classification are crucial for optimal management and improving patient outcomes.[84] In patients with ACLF, the cause of renal dysfunction differs from that in patients with decompensated cirrhosis, showing structural kidney injury through urinalysis and renal biomarkers.[85,86] Kidney involvement can often be managed medically, and renal failure is rarely considered a contraindication for LT. However, when kidney failure coexists with other organ failures, a careful evaluation is required to determine the appropriateness of simultaneous liver-kidney transplantation (SLKT).[87,88]

The Asian Pacific Association for the Study of the Liver (APASL) defines kidneys and the brain as "utility" organs, while circulation and respiration are considered organs of futility.[86,89] Factors that increase post-LT mortality include elevated lactate levels (>4 mmol/L), the need for renal replacement therapy (RRT) at the time of LT, and infections with multidrug-resistant organisms (MDROs) while awaiting LT.[90–94] Renal involvement is an independent predictor of poor outcomes after transplantation.[95–97] A study by Ayar *et al.*[97] had shown that mortality and graft survival in deceased donors were influenced by factors such as donor death from cardiac causes, a cyclosporine-based immunosuppressive regimen, donor age, serum creatinine levels at 6 months post-transplantation, and RRT prior to transplantation. Another study analyzed 4088

LT recipients with nonalcoholic steatohepatitis (NASH), categorizing them based on renal function. Recipients with preserved renal function (group 2) had a 19% lower risk of death with a functioning graft compared to those with severe renal dysfunction (group 1). SLKT recipients (group 3) had similar risks for graft loss but higher risk for death with a functioning graft. Pretransplant renal dysfunction in NASH patients was associated with worse post-LT outcomes.[98] The course of organ failure, particularly kidney failure, in the ICU is a key determinant of outcomes, with resolution of organ failures and proper infection management improving survival. The presence of acute tubular necrosis (ATN) compared to hepatorenal syndrome (HRS) is linked to poorer outcomes and a higher risk of chronic kidney disease (CKD) post-transplant.[99] Patients needing RRT for more than 30 days are candidates for SLKT. The number of elderly patients (70+ years) needing both liver and kidney transplants is rising due to metabolic-related liver disease. A study by Kaufman *et al.*[100] analyzed transplant outcomes from 2017 to 2022, comparing elderly patients undergoing simultaneous liver-kidney (SLK) transplants with those receiving only kidney transplants or kidney after LT. Elderly patients had lower survival rates, with 1-year survival at 82.9% and 3-year survival at 66.5%, compared to better outcomes in younger age groups. Kidney transplant outcomes were also poorer in older patients. Despite these challenges, the author concluded that age alone should not exclude patients from transplantation, and sequential kidney transplants after LT may reduce the risks of futile procedures. Another study had shown that among 331 dual-listed patients for SLKT, 52% died awaiting transplant, and 39% of SLKT recipients experienced delayed graft function (RAF). RAF recipients had higher MELD scores, longer hospital stays, and poorer survival, with pretransplant dialysis, kidney cold ischemia, and donor risk factors being key predictors.[101]

Additional factors, such as age over 65, frailty, alcohol use, mechanical ventilation duration, and comorbid cardiac diseases, increase the risk of renal dysfunction.[102] The CLIF-C ACLF score, with a value over 70, is useful for predicting futility in ACLF patients with kidney injury.[103]

Futility of LT in patients with obesity

Obesity is increasingly prevalent, particularly among LT candidates, due to sedentary lifestyles and the availability of unhealthy food. The management of obese LT candidates remains controversial, as BMI alone is not an ideal measure of surgical risk, affected by factors like ascites and fat distribution. While weight loss may improve surgical outcomes, it is difficult for patients and may lead to malnutrition or sarcopenic obesity. Some case series have explored bariatric surgery either pre-transplant or during surgery, but large controlled trials are lacking.[104] Obese individuals are more prone to cardiac complications, which can negatively impact post-LT outcomes, making cardiovascular evaluation mandatory during pre-transplant workup. A study from the United States Liver Transplant Center found similar graft survival in obese and non-obese patients, but obesity was linked to more wound infections, dehiscence, biliary leaks, and strictures post-surgery. Long-term, obesity increases the risk of metabolic syndrome-related complications.[105–107] Although data on inferior LT outcomes for Class II and III obesity is limited, it was concluded that obese patients face more technical difficulties, infections, and biliary complications after LT compared to those with normal BMI.

Consensus Statements: Futility of LT in Patients with Obesity

Statement	Level of evidence	Strength of recommendation
Presence of obesity of any severity should not be taken as sole criteria of futility for LT	Moderate	Strong
Patients with severe obesity may be associated with higher morbidity in comparison to non-obese patients subjected to LT.	High	Strong
Evaluation and control of associated metabolic risk factors, cardiovascular and pulmonary conditions before LT needs consideration in patients with obesity.	Low	Weak

LT: liver transplantation.

Consensus Statements: Futility of LT in kidney morbidities

Statement	Level of evidence	Strength of recommendation
Patients with severe azotemia, oliguria on renal replacement therapy with >4 organ failure assessed by CLIF-SOFA at any time point should be considered futile for LT	High	Strong
Renal failure occurring as a part of multiorgan failure in the context of uncontrolled multidrug resistant infections is futile and should be avoided.	Moderate	Strong

LT: liver transplantation.

Futility of LT in diabetes, retinopathy, and peripheral vascular disorders

Diabetes mellitus (DM) and cirrhosis frequently coexist, with diabetic patients often experiencing metabolic complications like neuropathy, gastroparesis, nephropathy, and CAD. These microvascular complications contribute to poorer long-term survival in diabetic patients compared to non-diabetics. Immunosuppressive therapy post LT can exacerbate diabetes and related complications, leading to even worse outcomes.[108,109] Studies have shown that patients with DM and peripheral vascular disease have higher mortality within six years compared to those with myocardial infarction.[110]

Most data on diabetes-related complications in LT patients is retrospective, indicating a need for more prospective studies. A study by Shields *et al.*[111] compared diabetic LT recipients with non-diabetics, revealing higher mortality in diabetic patients (36% vs. 9%, $P < 0.001$) and poorer patient and graft survival at 1 and 5 years. Similarly, Thuluvath *et al.*[112] reported a 34% survival rate in diabetic patients over five years, compared to 68% in non-diabetic patients. A UNOS database analysis from 1994 to 2001 confirmed that diabetic patients, particularly those on insulin, had lower survival rates after five years (57% vs. 67%).[113]

A meta-analysis of over 15,000 diabetic LT recipients found that diabetes increased the risk of death and graft failure by 40% and 28%, respectively.[114] In a U.S. study, diabetic patients had higher all-cause mortality (1.36 times) and cardiovascular mortality (2.52 times) than non-diabetics.[115] Non-responsive diabetic complications, such as autonomic dysfunction, neuropathy, retinopathy, and gastroparesis, lead to higher morbidity and mortality. While DM without these complications isn't a futility criterion, these complications should be evaluated as futility criteria for LT.[116,117]

mortality risk by approximately two-fold (RR: 2.01; 95% CI: 1.70–2.36). The findings highlight the significant association between sarcopenia and higher mortality in LT patients, suggesting the need for interventional studies to address and potentially reverse sarcopenia in this population.[119] Another meta-analysis of 25 studies involving 7760 LT patients found that 40.7% of patients had preoperative sarcopenia. Those with sarcopenia had lower 1-, 3-, and 5-year post-LT survival probabilities compared to those without sarcopenia ($P < 0.05$). Sarcopenia was associated with an increased post-LT mortality risk (adjusted hazard ratio: 1.58; 95% CI: 1.21–2.07) and longer ICU stays, higher risk of sepsis, and more severe complications. The study concludes that sarcopenia is prevalent in LT patients and is independently linked to higher mortality and poorer outcomes.[120] In an Indian study of 74 LT recipients, 27% (n = 20) had sarcopenia. Fifteen patients died within one year post-transplant, and sarcopenia was significantly associated with 1-year mortality ($P = 0.001$). The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of sarcopenia as a predictor were 60%, 81%, 45%, and 88%, respectively. Sarcopenia was identified as an independent predictor of mortality although factors like mechanical ventilation, hospital stay, and infection were not significantly linked to sarcopenia.[120] While OS is lower in sarcopenic patients compared to non-sarcopenic individuals, sarcopenia alone should not be considered a futility criterion for LT.[121–125]

Frailty, a state of vulnerability affecting multiple organ systems, is observed in 20–30% of patients on the LT waitlist and is linked to higher waitlist mortality and adverse outcomes.[126–128] A consensus panel recommends postponing or canceling transplantation in critically ill patients with cirrhosis and a clinical frailty score greater than 7, as transplantation in such cases may be considered futile.[129]

Consensus Statements: Futility of LT in diabetes and its complications

Statement	Level of evidence	Strength of recommendation
Patient with long standing diabetes and coexisting uncorrected metabolic comorbidities like severe cardiovascular, renal and/or diabetic complications(micro and macrovascular) in the same patient significantly increases the morbidity and mortality post transplantation and are risk factors for a futile transplant.	Moderate	Strong

LT: liver transplantation.

Futility of LT in sarcopenia, frailty and ECOG status

Sarcopenia is commonly seen in patients with cirrhosis and is associated with increased mortality both on the LT waitlist and post-transplant due to complications like sepsis.[118] A meta-analysis of 33 studies involving 12,137 LT patients found that sarcopenia increased

However, many frail patients suffer from extreme malnutrition and diminished physiological reserves, which can improve post-transplant. A study of 1166 cirrhotic patients undergoing LT showed that frailty was associated with longer hospital and ICU stays, as well as higher mortality. Despite these challenges, the 1-, 3-, and 5-year survival rates were 94%, 89%, and 84%, respectively, indicating that

transplant in frail patients is not futile.[130] A study of 1166 adult LT recipients found that 21% were frail pre-transplant, defined by a Liver Frailty Index (LFI) ≥ 4.5. Frail patients had a higher risk of post-LT mortality and greater healthcare utilization, including prolonged hospital stays and ICU admissions. After adjusting for other factors, frailty was associated with a 2.13-fold increased risk of post-LT death and higher odds of extended hospital stays. The findings suggest that addressing pre-LT frailty may improve post-transplant outcomes and reduce resource use.[131] ECOG performance scores, another indicator of poor physiological reserve, also correlate with prolonged hospital stays, increased renal failure, and infection risks, but not with mortality.[132] Similar to sarcopenia and frailty, poor ECOG scores should not be considered as sole indicators of futility in LT.

Consensus Statements: Futility of LT in Sarcopenia, Frailty, and ECOG Status

Statement	Level of evidence	Strength of recommendation
Sarcopenia and frailty as single criteria in the pre-transplant period should not be a criteria for futility. However, patients with clinical frailty score of >7 had poor outcome and need individualized assessment	Moderate	Strong
Performance status alone should not be a criteria for futility in LT	Low	Weak

LT: liver transplantation.

Futility of LT in Splanchnic vascular disorders and cirrhosis (hypercoagulable disorders)

Radiological interventions have improved long-term outcomes in Budd-Chiari syndrome (BCS) patients.[132–135] LT is considered for BCS patients unresponsive to radiological treatments or those with acute/ACLF, end-stage cirrhosis, or HCC.[135,136] Advances in LT techniques and the availability of newer drugs for managing hypercoagulable states have improved outcomes.[137] In a study of 46 LT recipients for BCS, the survival rates at 1, 5, 10, and 20 years were 87%, 83%, 76%, and 60%, respectively. These outcomes were slightly better than those for other LT indications at the center. Vascular events did not impact overall mortality, but patients with myeloproliferative disorders had worse survival rates.[138] Asl *et al.*[139] confirmed similar results in 108 patients with BCS undergoing LT. Decisions regarding LT futility in BCS depend on factors like surgical expertise, clinical severity, and patient compliance. PVT, once a contraindication for LT, is now managed with anticoagulation, TIPS, and surgical interventions, improving LT outcomes.

Consensus Statement: Futility of LT in Vascular Disorders of Liver

Statement	Level of evidence	Strength of recommendation
The decision for the futility of liver transplantation in vascular liver diseases needs to be individualized according to technical/anatomic aspects and the degree of control of the underlying hypercoagulable state. Insufficient inflow to potential allograft from possible collaterals makes an LT futile and should not be attempted.	Low	Weak

LT: liver transplantation.

Futility of LT in recipients with infections (fungal, bacterial, or viral)

Bacterial infections are common in cirrhotic patients awaiting LT, while fungal infections, though less frequent, carry higher short-term mortality.[140,141] With improved diagnostic tools and effective treatments, infections are rarely a contraindication for LT. However, infections leading to sepsis, organ dysfunction, or shock can delay transplantation.

Common bacterial infections that may delay or contraindicate LT include:

1. **Urosepsis**: In cases of uncomplicated UTI, LT can proceed safely.[142]
2. **Spontaneous Bacterial Peritonitis (SBP)**: Uncomplicated SBP requires 5 days of antimicrobial therapy. Patients may be reactivated on the waitlist after 48 h if their ascitic fluid PMN count decreases by >25% and no organ dysfunction is present.[143]
3. **Spontaneous Bacteremia**: Requires 7–14 days of therapy. If there's no organ dysfunction, the patient can be reactivated after two consecutive negative blood cultures.[140]
4. **Pneumonitis**: At least 7 days of treatment is needed, with documented improvement in clinical status and oxygenation.[144]
5. **Spontaneous Fungal Peritonitis (SFP) and Fungemia**: Patients should complete 2–3 weeks of antifungal therapy and have negative cultures 7 days after treatment.[145]
6. **Clostridium Difficile Diarrhea**: Requires 7 days of therapy, complete symptom resolution, normal WBC, and improving serum markers before re-assessment for LT.[146]

Infections must be managed appropriately before considering LT, with a sufficient gap between the end of treatment and reactivation on the waitlist.

Consensus Statements: Futility of LT in sepsis

Statement	Level of evidence	Strength of recommendation
Liver transplantation is futile in the presence of an untreated or inadequately treated bacterial or fungal infection with the exception of asymptomatic bacteriuria, localized biliary sepsis in a patient with PSC.	High	Strong
Liver transplantation is futile in the presence of any infection-producing organ dysfunction and/or hemodynamic compromise which does not improve with appropriate anti-microbial therapy and organ support.	High	Strong
Liver transplantation is futile in a patient with secondary biliary peritonitis or intra-abdominal sepsis, unless the same has been treated with suitable anti-microbials and/or surgical/radiological/endoscopic intervention. Transplant may be delayed in these patients till complete resolution of infection is documented.	Moderate	Weak
Liver transplantation is futile in a cirrhotic patient infected with pan-drug resistant organism [most commonly from *Enterobacteriacea* spp.]	Low	Weak

LT: liver transplantation.

Futility of LT in tropical infections

Tropical infections can impact LT in several ways, including:

1. **Infections in LT Recipients and Donors**: Tropical infections in patients or donors before and after LT require separate management from liver disease itself.
2. **Drug-Induced Liver Injury (DILI)**: Treating tropical infections may cause DILI, which can be managed by discontinuing the offending drug.
3. **LT for ACLF Due to Tropical Infections**: While rare, LT may be needed for ACLF caused by tropical infections, though management approaches remain consistent.
4. **ALF** due to Tropical Infections: Some tropical infections, like Dengue, Scrub Typhus, Leptospirosis, Malaria, Antitubercular medication induced ALF, insecticide poisoning and Typhoid fever, can cause ALF and may require LT in extreme cases and need assessment on patient to patient basis due to lack of published literature.

Additionally, post-transplantation concerns include infections from the donor graft or blood products, reactivation of latent infections, or acquisition of new infections after immunosuppression. Tropical infections may also cause liver failure, making LT a consideration.

Common Tropical Infections Leading to ALF:

- **COVID-19**: Though not strictly tropical, it is prevalent in tropical regions and has been associated with ALF and LT.[147–152]
- **Dengue**: Common in India, dengue can cause hepatitis and ALF, though LT is rarely indicated unless other organ systems are unaffected and death from liver failure is imminent.[153–157]
- **Leptospirosis**: Case reports suggest LT for ALF due to leptospirosis.[158,159]
- **Malaria, Typhoid Fever, Scrub Typhus**: These infections can rarely mimic ALF but, if the liver is the only organ involved, LT may be a viable option.[160–164]

In cases where the liver is the only organ affected and treatments fail, LT remains a possible solution.

Consensus Statements: Futility of LT in Tropical Infections

Statement	Level of evidence	Strength of recommendation
Liver transplantation may be considered in highly selected patients with tropical infections if considered lifesaving and with good expected outcomes. Futility criteria for such transplantation will be similar to that stated above for acute liver failure and acute or chronic liver failure.	Low	Weak

LT: liver transplantation.

Futility of LT in anatomical variations of recipients and donors

It was discussed again that contraindications for LT should also consider anatomical variations as futility. Anatomical variations are common in the right lobe, particularly in terms of vascular and biliary structures. However, with increasing experience, these variations can be managed with technical modifications decided on a case-by-case basis. The only contraindication is in cases with intraparenchymal origin of the anterior portal vein(s) in combination with similar biliary variants. Steatosis of >30% (LAI < −5), less than 30% of liver volume as the minimum requirement for a liver graft, and a single portal vein that does not divide into left and right were considered contraindications for LDLT.[165,166]

Futility of LT in Relation to social, Financial, and Family Support

LT requires a detailed psychosocial assessment, which should be conducted by a multi-disciplinary LT team consisting of social workers, mental health professionals, liaison psychiatrists, and individuals trained in addiction rehabilitation.[167] It was discussed in detail that all contraindications as determined by the multi-disciplinary team should be considered as futility for LT. Standards have been developed to promote equity, trust, and transparency between recipients and their providers. Key components of the assessment include social support, behavioral and substance abuse problems, and other comorbid psychiatric illnesses that affect graft survival after transplant. A lack of these supports contraindicates LT in these patients, as it hampers both patient and graft survival.[168,169] Addiction specialists identify slips (short intervals of drinking) and relapses, which indicate addictive drinking, and they assess various scores with domains like social isolation, failed rehabilitation, lack of insight into addiction, and other psychiatric comorbidities to identify patients who may relapse after LT.[170]

Consensus Statements: Futility of LT in Relation to Social, Financial, and Family Support

Statement	Level of evidence	Strength of recommendation
LT cannot be considered if psychosocial, financial, and family support is not available.	Moderate	Strong
LT will be futile among active drug abuse and significant psychiatric illness.	Moderate	Weak

LT: liver transplantation.

The Futility of LT in drug abuse, including alcohol use

Substance use disorders, defined by an inability to control substance use, result in impairment in daily, personal, and social responsibilities. Alcoholic liver disease (ALD) ranges from asymptomatic steatosis to hepatitis, cirrhosis, ACLF, and HCC. Key questions in LT for ALD include the impact of alcohol relapse, patient selection and timing for LT, complications specific to ALD, and whether severe alcoholic hepatitis (SAH) should be a contraindication for LT.

Dumortier *et al.*[171] outlined the negative effects of heavy alcohol use after LT, including graft injury, loss, or death. While mild relapse typically has no effect on graft survival, moderate relapse increases the risk of fibrosis and graft injury, and severe relapse can result in early mortality. Inadequate referral systems result in only 10% of patients with decompensated ALD cirrhosis being referred for LT, with only 4% placed on the waitlist and 1.2% undergoing transplantation, leading to an estimated 12,000 deaths annually due to poor referral practices.[172]

The "6-month rule" for alcohol abstinence before LT, meant to allow for liver recovery and reduce relapse risk, has been controversial. Some argue that patients may die before reaching 6 months, while others see liver function improvement within the first 3 months. In 2012, AASLD, EASL, UNOS, and the French Consensus Conference agreed that the 6-month abstinence should no longer be absolute.[173] Recent consensus suggests LT should be offered to all patients with end-stage liver disease if it improves life expectancy, regardless of etiology.[173–176] Post-LT, complete alcohol abstinence is recommended by most international guidelines.[177]

Guidelines for LT as a rescue therapy in SAH are unclear, as patients typically do not meet the 6-month abstinence rule and have a high risk of alcohol relapse. However, recent evidence supports LT as a viable cure, especially since there is no other effective treatment aside from corticosteroids. Without intervention, the short-term mortality in these patients is high (75–90%), with many dying within 2 months. Early identification of high-risk patients is crucial, and scoring models like Maddrey's discriminant function, MELD-Na, Glasgow Alcoholic Hepatitis Score, and the Lillie model are used for assessment.[178,179] Early LT is recommended after the first decompensating event that doesn't respond to medical therapy, provided there are no severe comorbidities and the patient is motivated for abstinence. In these cases, 6-month survival is 77% with LT versus 23% without it.[180] Studies have shown survival benefits with early LT compared to medical therapy alone,[181] and no significant difference in relapse rates between SAH and chronic alcoholic cirrhosis subgroups.

Regarding non-alcoholic substance use, relapse rates are 22% for cocaine, 11% for opioids, and 11% for other substances. Despite a 26.9% overall relapse rate, this does not affect survival,[182] so these patients should also have access to LT.

Futility of Liver Transplantation in Severe Alcoholic Hepatitis

Statement	Level of evidence	Strength of recommendation
Liver transplantation can be done in highly selected cases of severe alcoholic hepatitis who have failed medical therapy, provided they have been cleared by the transplant team, trained psychiatrist/addiction specialist, and social support staff, and have good family support	Moderate	Strong

(*Continued on next page*)

(*Continued*)

Statement	Level of evidence	Strength of recommendation
Re-transplantation should be considered futile in patients who continued to abuse alcohol and are not compliant to medications and regular medical check-ups/ hospital visit	Low	Strong

DECLARATION OF COMPETING INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

REFERENCES

1. Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of recommendations. *BMJ*. 2004;328:1490.
2. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008;336:924–926.
3. Gustot T, Fernandez J, Garcia E, et al. Clinical Course of acute-on-chronic liver failure syndrome and effects on prognosis. *Hepatol Baltim Md*. 2015;62:243–252.
4. Artru F, Louvet A, Ruiz I, et al. Liver transplantation in the most severely ill cirrhotic patients: a multicenter study in acute-on-chronic liver failure grade 3. *J Hepatol*. 2017;67:708–715.
5. Levesque E, Winter A, Noorah Z, et al. Impact of acute-on-chronic liver failure on 90-day mortality following a first liver transplantation. *Liver Int*. 2017;37:684–693.
6. Kling CE, Perkins JD, Biggins SW, Wall AE, Reyes JD. Building a utility-based liver allocation model in preparation for continuous distribution. *Transplant Direct*. 2022;13:e1282, 8.
7. Shazi L, Abbas Z. Ethical dilemmas related to living donor liver transplantation in Asia. *Ir J Med Sci*. 2019;188:1185–1189.
8. Linecker M, Krones T, Berg T, et al. Potentially inappropriate liver transplantation in the era of the "sickest first" policy - a search for the upper limits. *J Hepatol*. 2018;68:798–813.
9. Petrowsky H, Rana A, Kaldas FM, et al. Liver transplantation in highest acuity recipients: identifying factors to avoid futility. *Ann Surg*. 2014;259:1186–1194.
10. Michard B, Artzner T, Lebas B, et al. Liver transplantation in critically ill patients: preoperative predictive factors of post-transplant mortality to avoid futility. *Clin Transplant*. 2017;31.
11. Rolak S, Elhawary A, Diwan T, Watt KD. Futility and poor outcomes are not the same thing: a clinical perspective of refined outcomes definitions in liver transplantation. *Liver Transplant*. 2024;30:421–430, 1.
12. Final rule - OPTN. https://optn.transplant.hrsa.gov/about/final-rule/.
13. Jothimani D, Simon E, Palanichamy S, et al. Outcome of patients waitlisted for deceased donor liver transplantation during COVID-19 pandemic: a single-center experience. *J Clin Exp Hepatol*. 2023;13:601–607.
14. Jain M, Varghese J, Kedarishetty, et al. Incidence and risk factors for mortality in patients with cirrhosis awaiting liver transplantation. *Indian Journal of Transplantation*. 2019;13:210–215.
15. Figorilli F, Putignano A, Roux O, et al. Development of an organ failure score in acute liver failure for transplant selection and identification of patients at high risk of futility. *PLoS One*. 2017;12:e0188151.
16. Kumar R, Anand U, Priyadarshi RN. Liver transplantation in acute liver failure: dilemmas and challenges. *World J Transplant*. 2021;11:187–202.
17. Michard B, Artzner T, Lebas B, et al. Liver transplantation in critically ill patients: preoperative predictive factors of post-transplant mortality to avoid futility. *Clin Transplant*. 2017 Dec;31.
18. Anand AC, Nandi B, Acharya SK, et al. Erratum to "Indian national association for the study of liver consensus statement on acute liver failure (Part-2): management of acute liver failure". *J Clin Exp Hepatol*. 2020;10:477–517. J Clin Exp Hepatol. 2022;12:729-730.
19. Kadimella A, Kedarisetty CK, Raya R, et al. First report of two-stage living donor liver transplantation to avoid futility and ensure double equipoise in acute liver failure complicated by toxic liver syndrome. *J Clin Exp Hepatol*. 2024;14:101443.
20. Moreau R, Jalan R, Gines P, et al. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. *Gastroenterology*. 2013;144:1426–1437, 1437.e1-9.
21. O'Leary JG, Reddy KR, Garcia-Tsao G, et al. NACSELD acute-on-chronic liver failure (NACSELD-ACLF) score predicts 30-day survival in hospitalized patients with cirrhosis. *Hepatol Baltim Md*. 2018;67:2367–2374.
22. Sarin SK, Kedarisetty CK, Abbas Z, et al. Acute-on-chronic liver failure: consensus recommendations of the asian pacific association for the study of the liver (APASL) 2014. *Hepatol Int*. 2014;8:453–471.
23. Merion RM. When is a patient too well and when is a patient too sick for a liver transplant? *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2004;10(10 suppl 2):S69–S73.
24. Umgelter A, Lange K, Kornberg A, Büchler P, Friess H, Schmid RM. Orthotopic liver transplantation in critically ill cirrhotic patients with multi-organ failure: a single-center experience. *Transplant Proc*. 2011;43:3762–3768.
25. Thuluvath PJ, Thuluvath AJ, Hanish S, Savva Y. Liver transplantation in patients with multiple organ failures: feasibility and outcomes. *J Hepatol*. 2018;69:1047–1056.
26. Sundaram V, Shah P, Wong RJ, et al. Patients with acute on chronic liver failure grade 3 have greater 14-day waitlist mortality than status-1a patients. *Hepatol Baltim Md*. 2019;70:334–345.
27. Artzner T, Michard B, Weiss E, et al. Liver transplantation for critically ill cirrhotic patients: stratifying utility based on pretransplant factors. *Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg*. 2020;20:2437–2448.
28. Mazzaferro V, Bhoori S, Sposito C, et al. Milan criteria in liver transplantation for hepatocellular carcinoma: an evidence-based analysis of 15 years of experience. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2011;17(suppl 2):S44–S57.
29. Sundaram V, Patel S, Shetty K, et al. Multi-organ dysfunction and evaluation for liver transplantation (MODEL) Consortium. Risk factors for posttransplantation mortality in recipients with grade 3 acute-on-chronic liver failure: analysis of a North American Consortium. *Liver Transplant*. 2022;28:1078–1089.
30. Artru F, Sacleux SC, Ursic-Bedoya J, et al. Long-term outcome following liver transplantation of patients with ACLF grade 3. *J Hepatol*. 2025;82:62–71.
31. Sacleux SC, Ichaö P, Coilly A, et al. Liver transplant selection criteria and outcomes in critically ill patients with ACLF. *JHEP Rep*. 2023;6:100929.
32. Bernal W, Taylor R, Rowe IA, et al. Liver transplantation for critically ill patients with acute on chronic liver failure: a prospective

national programme of waitlist prioritisation. *Lancet Reg Health Eur*. 2024;46:101067.
33. Sundaram V, Kogachi S, Wong RJ, et al. Effect of the clinical course of acute-on-chronic liver failure prior to liver transplantation on post-transplant survival. *J Hepatol*. 2020;72:481–488.
34. Jin P, Zhang W, Sun L, et al. Improve the prediction of liver transplant mortality based on pre-transplant factors: a multi-center study from China: mortality prediction of LT. *Dig Liver Dis*. 2024;56:818–826.
35. Hong G, Suh KS, Suh SW, et al. Alpha-fetoprotein and (18)F-FDG positron emission tomography predict tumor recurrence better than Milan criteria in living donor liver transplantation. *J Hepatol*. 2016;64:852–859.
36. Mehta N, Heimbach J, Harnois DM, et al. Validation of a risk estimation of tumor recurrence after transplant (RETREAT) score for hepatocellular carcinoma recurrence after liver transplant. *JAMA Oncol*. 2017;3:493–500.
37. Mehta N, Dodge JL, Roberts JP, Yao FY. Validation of the prognostic power of the RETREAT score for hepatocellular carcinoma recurrence using the UNOS database. *Am J Transplant*. 2018;18:1206–1213.
38. Pawlik TM, Delman KA, Vauthey JN, et al. Tumor size predicts vascular invasion and histologic grade: implications for selection of surgical treatment for hepatocellular carcinoma. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2005;11:1086–1092.
39. Degroote H, Piñero F, Costentin C, et al. French-Italian-Belgium and Latin American collaborative group for HCC and liver transplantation. International study on the outcome of locoregional therapy for liver transplant in hepatocellular carcinoma beyond Milan criteria. *JHEP Rep*. 2021;3:100331.
40. Sinha J, Mehta N, Dodge JL, et al. Are there upper limits in tumor burden for down-staging of hepatocellular carcinoma to liver transplant? Analysis of the all-comers protocol. *Hepatology*. 2019;70:1185–1196.
41. Mehta N, Dodge JL, Grab JD, Yao FY. National experience on down-staging of hepatocellular carcinoma before liver transplant: influence of tumor burden, alpha-fetoprotein, and wait time. *Hepatology*. 2020;71:943–954.
42. Tan DJH, Lim WH, Yong JN, et al. UNOS down-staging criteria for liver transplantation of hepatocellular carcinoma: systematic review and meta-analysis of 25 studies. *Clin Gastroenterol Hepatol*. 2023;21:1475–1484.
43. Bhatti ABH, Naqvi W, Khan NY, et al. Living donor liver transplantation for advanced hepatocellular carcinoma including macrovascular invasion. *J Cancer Res Clin Oncol*. 2022;148:245–253.
44. Bhatti ABH, Qureshi AI, Tahir R, et al. When to call it off: defining transplant candidacy limits in liver donor liver transplantation for hepatocellular carcinoma. *BMC Cancer*. 2020;20:754.
45. Wai CT, Woon WA, Tan YM, et al. Younger age and presence of macrovascular invasion were independent significant factors associated with poor disease-free survival in hepatocellular carcinoma patients undergoing living donor liver transplantation. *Transplant Proc*. 2012;44:516–519.
46. De Vreede I, Steers JL, Burch PA, et al. Prolonged disease-free survival after orthotopic liver transplantation plus adjuvant chemoirradiation for cholangiocarcinoma. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2000;6:309–316.
47. Darwish Murad S, Kim WR, Therneau T, et al. Predictors of pretransplant dropout and posttransplant recurrence in patients with perihilar cholangiocarcinoma. *Hepatol Baltim Md*. 2012;56:972–981.
48. Le Treut YP, Grégoire E, Belghiti J, et al. Predictors of long-term survival after liver transplantation for metastatic endocrine tumors: an 85-case French multicentric report. *Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg*. 2008;8:1205–1213.
49. Gedaly R, Daily MF, Davenport D, et al. Liver transplantation for the treatment of liver metastases from neuroendocrine tumors: an analysis of the UNOS database. *Arch Surg Chic Ill*. 1960. 2011;146:953–958.
50. Nguyen NTT, Harring TR, Goss JA, O'Mahony CA. Neuroendocrine liver metastases and orthotopic liver transplantation: the US experience. *Int J Hepatol*. 2011;2011:742890.
51. Hagness M, Foss A, Line PD, et al. Liver transplantation for nonresectable liver metastases from colorectal cancer. *Ann Surg*. 2013;257:800–806.
52. Adam R, Piedvache C, Chiche L, et al. Collaborative TransMet group. Liver transplantation plus chemotherapy versus chemotherapy alone in patients with permanently unresectable colorectal liver metastases (TransMet): results from a multicentre, open-label, prospective, randomised controlled trial. *Lancet*. 2024;404:1107–1118.
53. Smedman TM, Line P, Hagness M, et al. Liver transplantation for unresectable colorectal liver metastases in patients and donors with extended criteria (SECA-II arm D study). *BJS Open*. 2020;4:467–477.
54. Ercolani G, Grazi GL, Pinna AD. Liver transplantation for benign hepatic tumors: a systematic review. *Dig Surg*. 2010;27:68–75.
55. Grossman EJ, Millis JM. Liver transplantation for non-hepatocellular carcinoma malignancy: indications, limitations, and analysis of the current literature. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2010;16:930–942.
56. Casey LC, Fontana RJ, Aday A, et al. Acute liver failure (ALF) in pregnancy: how much is pregnancy related? *Hepatol Baltim Md*. 2020;72:1366–1377.
57. Zarrinpar A, Farmer DG, Ghobrial RM, et al. Liver transplantation for HELLP syndrome. *Am Surg*. 2007;73:1013–1016.
58. Torres-Quevedo R, Moya-Herraiz A, San Juan F, et al. Indications for and results of liver retransplantation. *Transplant Proc*. 2009;41:1016–1017.
59. Adam R, Karam V, Delvart V, et al. Evolution of indications and results of liver transplantation in Europe. A report from the European Liver Transplant Registry (ELTR). *J Hepatol*. 2012;57:675–688.
60. Yoon PD, Patel MS, Murillo Perez CF, et al. Outcomes of adult liver retransplantation: a Canadian national database analysis. *Chin J Gastroenterol Hepatol*. 2022;2022:9932631.
61. Rosen HR, Prieto M, Casanovas-Taltavull T, et al. Validation and refinement of survival models for liver retransplantation. *Hepatol Baltim Md*. 2003;38:460–469.
62. Davis A, Rosenthal P, Glidden D. Pediatric liver retransplantation: outcomes and a prognostic scoring tool. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2009;15:199–207.
63. Brüggenwirth IMA, Werner MJM, Adam R, et al. The Liver Retransplantation Risk Score: a prognostic model for survival after adult liver retransplantation. *Transpl Int*. 2021;34:1928–1937.
64. Kuramitsu K, Fukumoto T, Egawa H, et al. A multicenter Japanese survey assessing the long-term outcomes of liver retransplantation using living donor grafts. *Transplantation*. 2020;104:754–761.
65. Zimmerman MA, Ghobrial RM. When shouldn't we retransplant? *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2005;(11 suppl 2):S14–S20.

66. Krendl FJ, Fodor M, Buch ML, et al. The BAR score predicts and stratifies outcomes following liver retransplantation: insights from a retrospective cohort study. *Transpl Int*. 2024;37:12104.
67. Skaro AI, Gallon LG, Lyuksemburg V, et al. The impact of coronary artery disease on outcomes after liver transplantation. *J Cardiovasc Med Hagerstown Md*. 2016;17:875–885.
68. Satapathy SK, Vanatta JM, Helmick RA, et al. Outcome of liver transplant recipients with revascularized coronary artery disease: a comparative analysis with and without cardiovascular risk factors. *Transplantation*. 2017;101:793–803.
69. Patel SS, Lin FP, Rodriguez VA, et al. The relationship between coronary artery disease and cardiovascular events early after liver transplantation. *Liver Int*. 2019;39:1363–1371.
70. VanWagner LB, Serper M, Kang R, et al. Factors associated with major adverse cardiovascular events after liver transplantation among a national sample. *Am J Transplant*. 2016;16:2684–2694.
71. Albeldawi M, Aggarwal A, Madhwal S, et al. Cumulative risk of cardiovascular events after orthotopic liver transplantation. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2012;18:370–375.
72. Fussner LA, Heimbach JK, Fan C, et al. Cardiovascular disease after liver transplantation: when, what, and who is at risk. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2015;21:889–896.
73. VanWagner LB, Ning H, Whitsett M, et al. A point-based prediction model for cardiovascular risk in orthotopic liver transplantation: the CAR-OLT score. *Hepatol Baltim Md*. 2017;66:1968–1979.
74. VanWagner LB, Harinstein ME, Runo JR, et al. Multidisciplinary approach to cardiac and pulmonary vascular disease risk assessment in liver transplantation: an evaluation of the evidence and consensus recommendations. *Am J Transplant*. 2018;18:30–42.
75. Levine GN, Bates ER, Bittl JA, et al. ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of cardiology/American heart association task force on clinical practice guidelines, 2016 *J Am Coll Cardiol*. 2016;68:1082–1115.
76. Izzy M, VanWagner LB, Lin G, et al. Redefining cirrhotic cardiomyopathy for the modern era. *Hepatol Baltim Md*. 2020;71:334–345.
77. Krowka MJ, Swanson KL, Frantz RP, McGoon MD, Wiesner RH. Portopulmonary hypertension: results from a 10-year screening algorithm. *Hepatol Baltim Md*. 2006;44:1502–1510.
78. Krowka MJ, Plevak DJ, Findlay JY, Rosen CB, Wiesner RH, Krom RA. Pulmonary hemodynamics and perioperative cardiopulmonary-related mortality in patients with portopulmonary hypertension undergoing liver transplantation. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2000;6:443–450.
79. Rybak D, Fallon MB, Krowka MJ, et al. Risk factors and impact of chronic obstructive pulmonary disease in candidates for liver transplantation. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2008;14:1357–1365.
80. Chung LP, Winship P, Phung S, Lake F, Waterer G. Five-year outcome in COPD patients after their first episode of acute exacerbation treated with non-invasive ventilation. *Respirol Carlton Vic*. 2010;15:1084–1091.
81. Seamark DA, Seamark CJ, Halpin DMG. Palliative care in chronic obstructive pulmonary disease: a review for clinicians. *J R Soc Med*. 2007;100:225–233.
82. Hwang S, Kim YH, Kim DK, et al. Resection of pulmonary metastases from hepatocellular carcinoma following liver transplantation. *World J Surg*. 2012;36:1592–1602.
83. Olson AL, Swigris JJ, Lezotte DC, Norris JM, Wilson CG, Brown KK. Mortality from pulmonary fibrosis increased in the United States from 1992 to 2003. *Am J Respir Crit Care Med*. 2007;176:277–284.
84. Nadim MK, Kellum JA, Forni L, et al. Acute kidney injury in patients with cirrhosis: acute Disease Quality Initiative (ADQI) and International Club of Ascites (ICA) joint multidisciplinary consensus meeting. *J Hepatol*. 2024;81:163–183.
85. Maiwall R, Pasupuleti SSR, Chandel SS, et al. Co-orchestration of acute kidney injury and non-kidney organ failures in critically ill patients with cirrhosis. *Liver Int*. 2021;41:1358–1369.
86. Maiwall R, Sarin SK, Moreau R. Acute kidney injury in acute on chronic liver failure. *Hepatol Int*. 2016;10:245–257.
87. Dube GK, Cohen DJ. Simultaneous liver and kidney transplantation. *Curr Opin Nephrol Hypertens*. 2007;16:547–553.
88. Grant L, Tujios S, Singal AG. Outcomes of simultaneous liver-kidney transplantation: implications for patient selection. *Curr Opin Organ Transplant*. 2018;23:264–270.
89. Sarin SK, Kumar A, Almeida JA, et al. Acute-on-chronic liver failure: consensus recommendations of the Asian Pacific Association for the study of the liver (APASL). *Hepatol Int*. 2009;3:269–282.
90. Zhang S, Suen SC, Gong CL, et al. Early transplantation maximizes survival in severe acute-on-chronic liver failure: results of a Markov decision process model. *JHEP Rep Innov Hepatol*. 2021;3:100367.
91. Goussous N, Xie W, Zhang T, et al. Acute on chronic liver failure: factors associated with transplantation. *Transplant Direct*. 2021;7:e788.
92. Belli LS, Duvoux C, Artzner T, et al. Liver transplantation for patients with acute-on-chronic liver failure (ACLF) in Europe: results of the ELITA/EF-CLIF collaborative study (ECLIS). *J Hepatol*. 2021;75:610–622.
93. Piano S, Singh V, Caraceni P, et al. Epidemiology and effects of bacterial infections in patients with cirrhosis worldwide. *Gastroenterology*. 2019;156:1368–1380.e10.
94. Choudhury A, Vijayaraghavan R, Maiwall R, et al. "First week" is the crucial period for deciding living donor liver transplantation in patients with acute-on-chronic liver failure. *Hepatol Int*. 2021;15:1376–1388.
95. Sundaram V, Jalan R, Wu T, et al. Factors associated with survival of patients with severe acute-on-chronic liver failure before and after liver transplantation. *Gastroenterology*. 2019;156:1381–1391.e3.
96. Sundaram V, Kogachi S, Wong RJ, et al. Effect of the clinical course of acute-on-chronic liver failure prior to liver transplantation on post-transplant survival. *J Hepatol*. 2020;72:481–488.
97. Ayar Y, Ersoy A, Ocakoglu G, et al. Risk factors affecting graft and patient survivals after transplantation from deceased donors in a developing country: a single-center experience. *Transplant Proc*. 2017 Mar;49:270–277.
98. Molnar MZ, Joglekar K, Jiang Y, et al. Global NAFLD Consortium. Association of pretransplant renal function with liver graft and patient survival after liver transplantation in patients with nonalcoholic steatohepatitis. *Liver Transplant*. 2019;25:399–410.
99. Nadim MK, Genyk YS, Tokin C, et al. Impact of the etiology of acute kidney injury on outcomes following liver transplantation: acute tubular necrosis versus hepatorenal syndrome. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2012;18:539–548.
100. Kaufman DM, Perkins JD, Bakthavatsalam R, Leca N, Sibulesky L. Simultaneous liver and kidney transplantation in patients aged 70 y and older: proceed with caution. *Transplant Direct*. 2024;10:e1683.

101. Lunsford KE, Bodzin AS, Markovic D, et al. Avoiding futility in simultaneous liver-kidney transplantation: analysis of 331 consecutive patients listed for dual organ replacement. *Ann Surg*. 2017;265:1016–1024.
102. Putignano A, Gustot T. New concepts in acute-on-chronic liver failure: implications for liver transplantation. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2017;23:234–243.
103. Engelmann C, Thomsen KL, Zakeri N, et al. Validation of CLIF-C ACLF score to define a threshold for futility of intensive care support for patients with acute-on-chronic liver failure. *Crit Care Lond Engl*. 2018;22:254.
104. Lazzati A, Iannelli A, Schneck AS, et al. Bariatric surgery and liver transplantation: a systematic review a new frontier for bariatric surgery. *Obes Surg*. 2015;25:134–142.
105. Dick AAS, Spitzer AL, Seifert CF, et al. Liver transplantation at the extremes of the body mass index. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2009;15:968–977.
106. Saab S, Lalezari D, Pruthi P, Alper T, Tong MJ. The impact of obesity on patient survival in liver transplant recipients: a meta-analysis. *Liver Int*. 2015;35:164–170.
107. Orci LA, Majno PE, Berney T, Morel P, Mentha G, Toso C. The impact of wait list body mass index changes on the outcome after liver transplantation. *Transpl Int*. 2013;26:170–176.
108. Modjtahedi BS, Wu J, Luong TQ, Gandhi NK, Fong DS, Chen W. Severity of diabetic retinopathy and the risk of future cerebrovascular disease, cardiovascular disease, and all-cause mortality. *Ophthalmology*. 2021;128:1169–1179.
109. Xu XH, Sun B, Zhong S, Wei DD, Hong Z, Dong AQ. Diabetic retinopathy predicts cardiovascular mortality in diabetes: a meta-analysis. *BMC Cardiovasc Disord*. 2020;20:478.
110. Caro J, Migliaccio-Walle K, Ishak KJ, Proskorovsky I. The morbidity and mortality following a diagnosis of peripheral arterial disease: long-term follow-up of a large database. *BMC Cardiovasc Disord*. 2005;5:14.
111. Shields PL, Tang H, Neuberger JM, Gunson BK, McMaster P, Pirenne J. Poor outcome in patients with diabetes mellitus undergoing liver transplantation. *Transplantation*. 1999;68:530–535.
112. John PR, Thuluvath PJ. Outcome of liver transplantation in patients with diabetes mellitus: a case-control study. *Hepatol Baltim Md*. 2001;34:889–895.
113. Yoo HY, Thuluvath PJ. The effect of insulin-dependent diabetes mellitus on outcome of liver transplantation. *Transplantation*. 2002;74:1007–1012.
114. Li P, Fan H, He Q. Pretransplant diabetes mellitus predicts worse outcomes of liver transplantation: evidence from meta-analysis. *J Endocrinol Investig*. 2018;41:211–221.
115. Yasodhara A, Dong V, Azhie A, Goldenberg A, Bhat M. Identifying modifiable predictors of long-term survival in liver transplant recipients with diabetes mellitus using machine learning. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2021;27:536–547.
116. Azevedo LDLS, Stucchi RSB, Ataíde ECD, Boin IFDF. Assessment of causes of early death after twenty years of liver transplantation. *Transplant Proc*. 2013;45:1116–1118.
117. Thuluvath PJ. When is diabetes mellitus a relative or absolute contraindication to liver transplantation? *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2005;(11 suppl 2):S25–S29.
118. Tandon P, Ney M, Irwin I, et al. Severe muscle depletion in patients on the liver transplant wait list: its prevalence and independent prognostic value. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2012;18:1209–1216.
119. Prokopidis K, Affronti M, Testa GD, et al. Sarcopenia increases mortality risk in liver transplantation: a systematic review and meta-analysis. *Panminerva Med*. 2024;66:47–54.
120. Kumar VV, Kothakota SR, Nair AK, et al. Impact of sarcopenia on post-liver transplant morbidity and mortality in cirrhotic patients. *Indian J Gastroenterol*. 2022;41:440–445.
121. Englesbe MJ, Patel SP, He K, et al. Sarcopenia and mortality after liver transplantation. *J Am Coll Surg*. 2010;211:271–278.
122. Lee CS, Cron DC, Terjimanian MN, et al. Dorsal muscle group area and surgical outcomes in liver transplantation. *Clin Transplant*. 2014;28:1092–1098.
123. Masuda T, Shirabe K, Ikegami T, et al. Sarcopenia is a prognostic factor in living donor liver transplantation. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2014;20:401–407.
124. Kumar V, Benjamin J, Shasthry V, et al. Sarcopenia in cirrhosis: fallout on liver transplantation. *J Clin Exp Hepatol*. 2020;10:467–476.
125. Tan Y, Duan T, Li B, et al. Sarcopenia defined by psoas muscle index independently predicts long-term survival after living donor liver transplantation in male recipients. *Quant Imag Med Surg*. 2022;12:215–228.
126. Lai JC, Feng S, Terrault NA, Lizaola B, Hayssen H, Covinsky K. Frailty predicts waitlist mortality in liver transplant candidates. *Am J Transplant*. 2014;14:1870–1879.
127. Lai JC, Rahimi RS, Verna EC, et al. Frailty associated with waitlist mortality independent of ascites and hepatic encephalopathy in a multicenter study. *Gastroenterology*. 2019;156:1675–1682.
128. Wang S, Whitlock R, Xu C, et al. Frailty is associated with increased risk of cirrhosis disease progression and death. *Hepatol Baltim Md*. 2022;75:600–609.
129. Weiss E, Saner F, Asrani SK, et al. When is a critically ill cirrhotic patient too sick to transplant? Development of consensus criteria by a multidisciplinary panel of 35 international experts. *Transplantation*. 2021;105:561–568.
130. Lai JC, Shui AM, Duarte-Rojo A, et al. Frailty, mortality, and health care utilization after liver transplantation: from the multicenter functional assessment in liver transplantation (FrAILT) study. *Hepatol Baltim Md*. 2022;75:1471–1479.
131. Lai JC, Shui AM, Duarte-Rojo A, et al. From the multi-center functional assessment in liver transplantation (FrAILT) study. Frailty, mortality, and health care utilization after liver transplantation: from the multicenter functional assessment in liver transplantation (FrAILT) study. *Hepatology*. 2022;75:1471–1479.
132. Wallace D, Cowling TE, Walker K, et al. The impact of performance status on length of hospital stay and clinical complications following liver transplantation. *Transplantation*. 2021;105:2037–2044.
133. Hemachandran N, Shalimar null, Acharya S, et al. Long-term outcomes of endovascular interventions in more than 500 patients with budd-Chiari syndrome. *J Vasc Interv Radiol JVIR*. 2021;32:61–69.e1.
134. Shalimar null, Kumar A, Kedia S, et al. Hepatic venous outflow tract obstruction: treatment outcomes and development of a new prognostic score. *Aliment Pharmacol Ther*. 2016;43:1154–1167.
135. Northup PG, Garcia-Pagan JC, Garcia-Tsao G, et al. Vascular liver disorders, portal vein thrombosis, and procedural bleeding in patients with liver disease: 2020 practice guidance by the American association for the study of liver diseases. *Hepatol Baltim Md*. 2021;73:366–413.
136. null Shalimar, Sharma S, Gamanagatti SR, et al. Acute-on-Chronic liver failure in Budd-Chiari syndrome: profile and predictors of outcome. *Dig Dis Sci*. 2020;65:2719–2729.

137. Singer AL, Locke JE, Stewart ZA, et al. Successful liver transplantation for Budd-Chiari syndrome in a patient with paroxysmal nocturnal hemoglobinuria treated with the anti-complement antibody eculizumab. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2009;15:540–543.
138. Ibach M, Eurich D, Dobrindt E, et al. Orthotopic liver transplantation for budd-Chiari syndrome: observations from a 30-year liver transplant program. *Medicina*. 2021;57:821.
139. Asl AA, Lankarani KB, Nikeghbalian S, et al. Post liver transplant complications of Budd-Chiari syndrome. *Indian J Gastroenterol*. 2021;40:281–286.
140. Jalan R, Fernandez J, Wiest R, et al. Bacterial infections in cirrhosis: a position statement based on the EASL Special Conference 2013. *J Hepatol*. 2014;60:1310–1324. https://doi.org/10.1016/j.jhep.2014.01.024.
141. Fernández J, Acevedo J, Wiest R, et al. Bacterial and fungal infections in acute-on-chronic liver failure: prevalence, characteristics and impact on prognosis. *Gut*. 2018;67:1870–1880.
142. Wong F, Piano S, Singh V, et al. Clinical features and evolution of bacterial infection-related acute-on-chronic liver failure. *J Hepatol*. 2021;74:330–339.
143. Piano S, Fasolato S, Salinas F, et al. The empirical antibiotic treatment of nosocomial spontaneous bacterial peritonitis: results of a randomized, controlled clinical trial. *Hepatol Baltim Md*. 2016;63:1299–1309.
144. Viasus D, Garcia-Vidal C, Castellote J, et al. Community-acquired pneumonia in patients with liver cirrhosis: clinical features, outcomes, and usefulness of severity scores. *Medicine (Baltim)*. 2011;90:110–118.
145. Pappas PG, Kauffman CA, Andes DR, et al. Clinical practice guideline for the management of candidiasis: 2016 update by the infectious diseases society of America. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2016;62:e1–e50.
146. Luo R, Weinberg JM, Barlam TF. The impact of Clostridium difficile infection on future outcomes of solid organ transplant recipients. *Infect Control Hosp Epidemiol*. 2018;39:563–570.
147. Gholami N, Amzajerdi VS, Mehdioghli R, Heris HK, Kazempour MJ. Isolated hyperbilirubinemia as the manifestation of acute liver failure in a patient with acute myelogenous leukemia and COVID-19 infection. *Eur J Transl Myol*. 2021;31:9817.
148. Pellegrini JR, Sabbula B, Russe-Russe JR, et al. A retrospective analysis of COVID-19-infected patients with acute hepatitis who develop acute liver failure in a safety net hospital. *BMJ Open Gastroenterol*. 2021;8:e000738.
149. Gurala D, Al Moussawi H, Philipose J, Abergel JR. Acute liver failure in a COVID-19 patient without any preexisting liver disease. *Cureus*. 2020;12:e10045.
150. Sohrabi M, SobheRakhshankhah E, Ziaei H, AtaeeKachuee M, Zamani F. Acute liver failure after vaccination against of COVID-19; a case report and review literature. *Respir Med Case Rep*. 2022;35:101568.
151. Carothers C, Birrer K, Vo M. Acetylcysteine for the treatment of suspected remdesivir-associated acute liver failure in COVID-19: a case series. *Pharmacotherapy*. 2020;40:1166–1171.
152. Kidson KM, Park J, Charles MK, et al. Successful liver transplantation in a patient with acute COVID-19 infection and acute liver failure: a case report. *Transplant Direct*. 2021;7:e747.
153. Devarbhavi H, Ganga D, Menon M, Kothari K, Singh R. Dengue hepatitis with acute liver failure: clinical, biochemical, histopathological characteristics and predictors of outcome. *J Gastroenterol Hepatol*. 2020;35:1223–1228.
154. Chikkala BR, Pandey Y, Acharya R, et al. Living donor liver transplant for dengue-related acute liver failure: a case report. *Exp Clin Transplant*. 2021;19:163–166.
155. Teerasarntipan T, Chaiteerakij R, Komolmit P, Tangkijvanich P, Treeprasertsuk S. Acute liver failure and death predictors in patients with dengue-induced severe hepatitis. *World J Gastroenterol*. 2020;26:4983–4995.
156. Tafere GG, Wondafrash DZ, Demoz FB. Repurposing of N-acetylcysteine for the treatment of dengue virus-induced acute liver failure. *Hepatic Med*. 2020;12:173–178.
157. Anand AC, Nandi B, Acharya SK, et al. Indian national association for the study of liver consensus statement on acute liver failure (Part-2): management of acute liver failure. *J Clin Exp Hepatol*. 2020;10:477–517.
158. Chavez-Iniguez JS, Cabrera-Aguilar S, Garcia-Garcia G, Armendariz-Borunda J. Acute kidney injury and acute liver failure in Leptospira infection and Weil's syndrome. *J Ren Hepatic Disord*. 2020;4:21–28.
159. Karvellas CJ, Francoz C, Weiss E. Liver transplantation in acute-on-chronic liver failure. *Transplantation*. 2021;105:1471–1481.
160. Lebreton T, Aubrun F, Mabrut JY, Heyer L, Perrin C. Liver transplantation for acute liver failure attributed to leptospirosis: a report of two cases. *Case Rep Crit Care*. 2019;2019:5189542.
161. Anand AC, Garg HK. Approach to clinical syndrome of jaundice and encephalopathy in tropics. *J Clin Exp Hepatol*. 2015;5(suppl 1):S116–S130.
162. Gaba S, Sharma S, Gaba N, Gupta M. Scrub typhus leading to acute liver failure in a pregnant patient. *Cureus*. 2020;12:e10191.
163. Verma N, Sharma M, Biswal M, et al. Hepatitis E Virus induced acute liver failure with Scrub typhus coinfection in a pregnant woman. *J Clin Exp Hepatol*. 2017;7:158–160.
164. Goswami D, Hing A, Das A, Lyngdoh M. Scrub typhus complicated by acute respiratory distress syndrome and acute liver failure: a case report from Northeast India. *Int J Infect Dis IJID Off Publ Int Soc Infect Dis*. 2013;17:e644–e645.
165. Soin AS, Chaudhary RJ, Pahari H, Pomfret EA. A worldwide survey of live liver donor selection policies at 24 centers with a combined experience of 19 009 adult living donor liver transplants. *Transplantation*. 2019;103:e39–e47.
166. Narasimhan G, Safwan M, Kota V, et al. Donor outcomes in living donor liver transplantation-analysis of 275 donors from a single centre in India. *Transplantation*. 2016;100:1251–1256.
167. Martin P, DiMartini A, Feng S, Brown R, Fallon M. Evaluation for liver transplantation in adults: 2013 practice guideline by the American association for the study of liver diseases and the American society of transplantation. *Hepatol Baltim Md*. 2014;59:1144–1165.
168. Weinrieb RM, Van Horn DH, McLellan AT, Lucey MR. Interpreting the significance of drinking by alcohol-dependent liver transplant patients: fostering candor is the key to recovery. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2000;6:769–776.
169. Dobbels F, Vanhaecke J, Dupont L, et al. Pretransplant predictors of posttransplant adherence and clinical outcome: an evidence base for pretransplant psychosocial screening. *Transplantation*. 2009;87:1497–1504.
170. Shen NT, Shenoy A, Brown RS, Verna EC. Identifying risk of alcohol relapse after liver transplantation: what tools do we need? *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc*. 2019;25:1133–1135.
171. Dumortier J, Guillaud O, Adham M, et al. Negative impact of de novo malignancies rather than alcohol relapse on survival after liver transplantation for alcoholic cirrhosis: a retrospective analysis of 305 patients in a single center. *Am J Gastroenterol*. 2007;102:1032–1041.

172. Kotlyar DS, Burke A, Campbell MS, Weinrieb RM. A critical review of candidacy for orthotopic liver transplantation in alcoholic liver disease. *Am J Gastroenterol*. 2008;103:734–743.
173. European Association for the Study of Liver. EASL clinical practical guidelines: management of alcoholic liver disease. *J Hepatol*. 2012;57:399–420.
174. Merion RM, Schaubel DE, Dykstra DM, Freeman RB, Port FK, Wolfe RA. The survival benefit of liver transplantation. *Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg*. 2005;5:307–313.
175. Addolorato G, Bataller R, Burra P, et al. Liver transplantation for alcoholic liver disease. *Transplantation*. 2016;100:981–987.
176. Gallegos-Orozco JF, Charlton MR. Alcoholic liver disease and liver transplantation. *Clin Liver Dis*. 2016;20:521–534.
177. European Association for the Study of the Liver. European association for the study of the liver. EASL clinical practice guidelines: management of alcohol-related liver disease. *J Hepatol*. 2018;69:154–181.
178. Papastergiou V, Tsochatzis EA, Pieri G, et al. Nine scoring models for short-term mortality in alcoholic hepatitis: cross-validation in a biopsy-proven cohort. *Aliment Pharmacol Ther*. 2014;39:721–732.
179. Louvet A, Naveau S, Abdelnour M, et al. The Lille model: a new tool for therapeutic strategy in patients with severe alcoholic hepatitis treated with steroids. *Hepatol Baltim Md*. 2007;45:1348–1354.
180. Mathurin P, Moreno C, Samuel D, et al. Early liver transplantation for severe alcoholic hepatitis. *N Engl J Med*. 2011;365:1790–1800.
181. Al-Saeedi M, Barout MH, Probst P, et al. Meta-analysis of patient survival and rate of alcohol relapse in liver-transplanted patients for acute alcoholic hepatitis. *Langenbecks Arch Surg*. 2018;403:825–836.
182. Nickels M, Jain A, Sharma R, et al. Polysubstance abuse in liver transplant patients and its impact on survival outcome. *Exp Clin Transplant*. 2007;5:680–685.