

An overview of unresolved issues in the perioperative management of liver transplant patients

Saurabh Mittal¹, Medha Bhardwaj², Praveenkumar Shekhrajka³, Vipin Kumar Goyal¹, Ganesh Ramaji Nimje¹, Sakshi Kanoji¹, Suma Katyaeni Danduri¹, Anshul Vishnoi¹

Received October 26, 2023

Revised November 20, 2023

Accepted November 21, 2023

Corresponding author: Vipin Kumar Goyal
Department of Organ Transplant
Anaesthesiology and Critical Care,
Mahatma Gandhi Medical College and
Hospital, Sitapura, Jaipur 302022, India
E-mail: dr.vipin28@gmail.com

¹Department of Organ Transplant Anaesthesiology and Critical Care, Mahatma Gandhi Medical College and Hospital, Jaipur, India

²Department of Neuro-Anaesthesia, Mahatma Gandhi Medical College and Hospital, Jaipur, India

³Department of Anaesthesia, Mahatma Gandhi Medical College and Hospital, Jaipur, India

Over the past decade, the field of solid organ transplantation has undergone significant changes, with some of the most notable advancements occurring in liver transplantation. Recent years have seen substantial progress in preoperative patient optimization protocols, anesthesia monitoring, coagulation management, and fluid management, among other areas. These improvements have led to excellent perioperative outcomes for all surgical patients, including those undergoing liver transplantation. In the last few decades, there have been numerous publications in the field of liver transplantation, but controversies related to perioperative management of liver transplant recipients persist. In this review article, we address the unresolved issues surrounding the anesthetic management of patients scheduled for liver transplantation.

Keywords: Coronary artery disease; End-stage liver disease; Intracranial pressure; Liver transplantation; Pulmonary hypertension

INTRODUCTION

Over the past decade, the field of solid organ transplantation has undergone significant changes, with some of the most notable advancements occurring in liver transplantation. Currently, liver transplantation is recognized as the optimal treatment for patients with end-stage liver disease (ESLD) caused by conditions such as alcoholic hepatitis, nonalcoholic steatohepatitis, viral hepatitis, hepatocellular carcinoma, acute fulminant hepatic failure, and hilar cholangiocarcinoma. Recent improvements in perioperative management have led to outstanding survival rates for liver transplant recipients. However, there remain several areas of debate concerning the periop-

erative anesthesia management of patients during liver transplantation. This review addresses the ongoing unresolved issues surrounding the anesthetic management of individuals scheduled for liver transplantation.

PREOPERATIVE EVALUATION OF THE CARDIOVASCULAR SYSTEM

Cardiovascular diseases, such as coronary artery disease, cirrhotic cardiomyopathy, valvular heart disease, and arrhythmias, are commonly identified during the preoperative work-up for liver transplantation. Coronary artery disease

HIGHLIGHTS

- In recent years, significant advancements have been made in preoperative patient optimization protocols, anesthesia monitoring, coagulation management, and fluid management.
- These improvements have led to excellent perioperative outcomes for all surgical patients, including those undergoing liver transplantation.
- Some unresolved issues still exist regarding perioperative anesthesia in patients during liver transplantation.

is particularly prevalent among patients scheduled for liver transplantation, and its incidence is on the rise. This increase is attributed to the growing acceptance of older recipients and the rising incidence of nonalcoholic steatohepatitis leading to liver failure [1]. Cirrhotic cardiomyopathy is a distinctive sequela of long-standing liver disease defined as systolic dysfunction (ejection fraction $\leq 50\%$ or global longitudinal strain $< 18\%$ or $> 22\%$) and diastolic dysfunction (≥ 3 of any of the following: septal e' velocity < 7 cm/s, E/e' ratio ≥ 15 , left atrial volume index [LAVI] > 34 mL/m², tricuspid regurgitation [TR] velocity > 2.8 m/s). Although patients with cirrhotic cardiomyopathy, are asymptomatic at rest, heart failure is quite high in these patients during stress, such as liver transplantation [2]. Even recipients with a normal ejection fraction but high probability score (Heart Failure Association–PEFF diagnostic score 5–6) due to preoperative risk factors such as advanced age, female sex, anemia, hypertension, or dyslipidemia is associated with an increased risk of postoperative heart failure with preserved ejection fraction (HFpEF) and poor long-term survival after liver transplantation [3]. Salah et al. [4] also concluded that nonalcoholic fatty liver disease (NAFLD) is closely associated with the development and progression of HFpEF, and further studies are required for screening, risk stratification, and establishing the impact on clinical outcomes.

Cardiac events, including left ventricular failure, myocardial infarction, fatal arrhythmias, and sudden cardiac arrest, are major contributors to perioperative mortality and morbidity among liver transplant recipients [5]. Therefore, preoperative cardiac evaluation and optimization are essential for patients with ESLD and necessitate the collaborative efforts of cardiologists, anesthesiologists, and hepatologists from the outset. Given these patients'

limited physical capacity, noninvasive screening tests such as electrocardiography (ECG), 2-dimensional echocardiography, and cardiac stress testing are routinely performed before transplantation at most centers. However, the efficacy of these cardiac screening tests has been called into question due to their low sensitivity and specificity in ESLD patients and the poor correlation with postoperative cardiac outcomes. QT prolongation, observed in approximately 40%–55% of ESLD patients on ECG, has limited prognostic value. Moreover, several confounders, including hypothyroidism, electrolyte abnormalities, obesity, and certain medications, can also prolong the QT interval [6]. Dobutamine stress echocardiography often yields false-negative results in patients with cirrhosis due to a blunted inotropic response, resulting in a low negative predictive value [7]. An elevated level of postoperative B-type natriuretic peptide (BNP) has been associated with high postoperative mortality. Although increased post-liver transplant BNP is multifactorial, a high preoperative BNP level is closely linked and can help in risk stratification before transplantation [8]. Consequently, the ideal screening tool for cardiovascular assessment prior to liver transplantation remains uncertain. Additionally, the appropriate frequency of cardiac risk assessment for patients on the waiting list is a contentious issue. Recent evidence has begun to support the use of invasive or non-invasive coronary angiography, which has proven to be more accurate in diagnosing coronary artery disease in ESLD patients with minimal or no risk [9,10].

Portopulmonary hypertension is a complication associated with long-standing ESLD. It is characterized by a mean pulmonary artery pressure of 25 mmHg or greater, increased pulmonary vascular resistance exceeding 240 dyne·sec/cm⁵, and a normal pulmonary capillary wedge pressure. Historically, moderate to severe pulmonary hypertension has been viewed as a contraindication for liver transplantation due to the high risk of postoperative mortality. For patients exhibiting a right ventricular systolic pressure greater than 45 mmHg on preoperative echocardiography, right heart catheterization is advised. While newer or smaller-volume centers may be reluctant to proceed with transplant in patients with moderate pulmonary arterial hypertension, some larger, experienced centers have begun to accept these patients and report satisfactory postoperative outcomes [11].

HEMODYNAMIC MONITORING

Patients undergoing liver transplantation may experience significant hemodynamic fluctuations during the intraoperative period. These fluctuations are particularly notable during the drainage of ascites, manipulation of the liver, clamping of major vessels such as the inferior vena cava or portal vein, acute major bleeding, and reperfusion of the grafted liver. Intraoperative hypotension and inadequate fluid management can accelerate the postoperative risk of complications, including acute kidney injury, the need for renal replacement therapy, poor graft function, graft failure, and sepsis. These complications can lead to increased morbidity and mortality among recipients [12–14]. Various monitoring parameters and devices are utilized during liver transplantation, including invasive blood pressure monitoring, pulmonary artery catheters, arterial pulse wave analysis (measuring pulse pressure variation [PPV] and stroke volume variation [SVV]), and transesophageal echocardiography (TEE). Each of these monitoring tools has its advantages and disadvantages. Therefore, perioperative hemodynamic monitoring should be tailored to the individual, taking into account the availability of equipment, patient-specific factors, and the knowledge and experience of the operator.

Although the pulmonary artery catheter (PAC) has been considered the gold standard for cardiac output (CO) monitoring, its utility for fluid management during liver transplantation has been challenged by numerous studies. Central venous pressure (CVP) and pulmonary artery occlusion pressure, when measured with a PAC during liver transplantation, have shown poor correlation with cardiac index or stroke volume index [15,16]. Consequently, the use of PAC in liver transplant surgery is generally reserved for patients with pulmonary hypertension, where monitoring pulmonary artery pressures is essential. Minimally invasive techniques, such as PiCCO, LiDCO plus, or EV1000/Vigileo, can estimate CO by analyzing pulse waves. However, these methods are not considered reliable in patients with advanced cirrhosis. A poor correlation between CO measurements obtained through pulse wave analysis and those obtained via PAC thermodilution techniques has been documented in patients undergoing liver transplantation [17,18]. Pulse wave analysis techniques also measure SVV and PPV, which can indicate fluid responsiveness during surgery and in the critical care setting. In the context of liver transplantation, both SVV and PPV have been identified as good predictors of

preload, specifically the right ventricular end-diastolic volume index [19,20]. However, there are several confounding factors that can affect these measurements, including spontaneous ventilation, a tidal volume less than 8 mL/kg, an open thorax, high positive end-expiratory pressure, and arrhythmias. These factors must be considered and addressed during monitoring.

Intraoperative TEE enables the rapid diagnosis of life-threatening conditions such as pulmonary thromboembolism, right ventricular failure, and regional wall motion abnormalities. It also provides a visual estimation of preload and ventricular function, which assists in guiding the administration of fluids and cardiac medications, including inotropes and vasopressors. Additionally, TEE offers real-time imaging of the hepatic and portal veins, allowing the direct visualization of any stenosis or thrombosis at the anastomosis site [21,22]. Although the routine use of TEE is on the rise among transplant centers, its application remains limited by the need for technical expertise, operator dependency, and the risk of bleeding, particularly in patients with grade 3 or 4 esophageal varices [23].

FLUID MANAGEMENT

During liver transplantation, aiming for a low CVP (<5 mmHg) to guide fluid administration can decrease intraoperative transfusion requirements. However, this practice is associated with an increased risk of postoperative renal failure. Conversely, a high CVP (>10 mmHg) is linked to a greater incidence of postoperative respiratory complications, longer intensive care unit stays, and higher mortality rates [24,25]. Recently, a moderately restrictive fluid therapy approach, combined with maintaining a mean arterial pressure >60–65 mmHg, has been recommended to reduce blood loss during the dissection phase. This can be achieved by maintaining a subnormal CVP (5–7 mmHg) and administering mild to moderate doses of vasopressors. Clinical consequences typically associated with hypervolemia, such as increased blood loss, the need for transfusions, and postoperative respiratory complications, are minimized with this approach, and there is no increased risk of acute kidney injury [26].

The choice of fluid—whether crystalloids or colloids—continues to be a topic of debate. Crystalloid options include 0.9% saline, 0.45% saline, dextrose in normal saline,

and balanced salt solutions (such as Ringer's lactate or Plasmalyte-A), each with its own benefits and limitations. In patients with preoperative hyponatremia, administering a large volume of 0.9% saline can cause a rapid increase in serum sodium levels, potentially leading to osmotic demyelination syndrome. Additionally, hyperchloremia from saline has been implicated in causing acidosis, hyperkalemia, and a decrease in the glomerular filtration rate due to afferent renal vasoconstriction. Ringer's lactate is typically avoided because of the risk of lactic acidosis and its potential to interfere with the assessment of a newly implanted graft. Most transplant centers prefer balanced salt solutions with low chloride content, which offer advantages such as acetate as a nonhepatic metabolized buffer, physiological chloride levels, and iso-osmolality. However, a recent high-quality, multicentric, randomized trial comparing balanced salt solutions with saline found no difference in 90-day survival or kidney injury, despite the expected increase in serum sodium levels in the saline group [26,27].

The preferred choice of colloid solution—starch gelatin or albumin—for the perioperative period remains a subject of debate, with transplant anesthesiologists adopting varying practices. Numerous studies have identified the detrimental effects of starches in perioperative and intensive care settings. Starches have been associated with an increased risk of postoperative acute kidney injury and coagulopathy, suggesting they are best avoided. Conversely, human albumin has been shown to reduce the total intravenous fluid requirement, the incidence of pulmonary and interstitial edema, postreperfusion syndrome, vasopressor requirements, and mortality. However, its widespread use is limited by the high cost, particularly in low-income countries [26].

COAGULATION MANAGEMENT

Packed red blood cells (PRBCs) and blood products such as fibrinogen concentrate, fresh frozen plasma, cryoprecipitate, and platelet concentrate must be reserved in advance of liver transplantation to ensure their availability when needed. The emerging theories on coagulation in patients with ESLD have shifted the paradigm concerning their bleeding tendencies. "Rebalanced coagulation" describes a delicate equilibrium between reduced levels of procoagulant and anticoagulant factors. The utility of

traditional coagulation parameters (prothrombin time [PT]/international normalized ratio [INR], activated partial thromboplastin time (aPTT), and fibrinogen) in perioperative coagulation management is debated due to their static nature, the time and resources required for testing, and their poor correlation with surgical bleeding. The use of point-of-care viscoelastic coagulation tests, such as thromboelastography or rotational thromboelastometry, has been shown to decrease perioperative transfusion requirements. These tests are now routinely incorporated into intraoperative coagulation management at most centers [28]. Studies have demonstrated that while perioperative point-of-care coagulation monitoring during liver transplantation can reduce the transfusion of red cells and other factor concentrates, it does not confer any benefit in terms of survival or other outcomes [29,30].

Despite elevated PT/INR levels and reduced platelet counts, many patients with acute or chronic liver disease exhibit normal ranges on viscoelastic tests. This aligns with the concept of rebalanced hemostasis, allowing these individuals to undergo liver transplantation without the need for blood product transfusions. Additionally, these tests can reveal further details such as hypercoagulability, a prothrombotic state, and the presence of endogenous heparinoids, which are associated with vascular endothelial damage [31]. No correlation was found between bleeding and coagulation defects. Consequently, prior to liver transplantation, correcting coagulation defects with plasma is deemed neither beneficial nor necessary [32]. Furthermore, plasma transfusion aimed at correcting coagulation defects does not reduce the need for intraoperative red cell transfusions during liver transplantation and may, in some cases, have the opposite effect [33].

Tranexamic acid appears to be effective in reducing the need for red blood cell transfusions without increasing the incidence of thromboembolic events across a broad spectrum of liver transplant recipients. This includes patients at low risk of intraoperative bleeding as well as those at high risk of complications such as thromboembolism. There is no indication that the use of tranexamic acid elevates the risk of thrombotic complications [34].

To date, no transfusion guidelines have been established for liver transplantation. However, bleeding during these procedures has significantly declined over time, enabling the performance of transfusion-free liver transplants. Synthetic factors, such as prothrombin complex concentrate, fibrinogen concentrate, and antifibrinolytics,

are increasingly being used as alternatives to the transfusion of blood and blood products. Administering platelets in the absence of bleeding or clinical coagulopathy may actually elevate the risk of adverse outcomes [34].

INTRACRANIAL PRESSURE MONITORING IN ACUTE LIVER FAILURE

In patients with acute liver failure (ALF), cerebral edema is present in nearly 80% of cases, leading to increased intracranial pressure (ICP) [35]. As edema worsens, the grade of encephalopathy also increases. Several mechanisms have been suggested to contribute to the development of brain edema, including cytotoxic edema and astrocyte swelling, ammonia-induced toxicity with resultant oxidative stress, and neuroinflammatory mediators such as interleukins and tumor necrosis factor alpha [36–39]. More recent studies incorporating radiological imaging have identified the coexistence of interstitial and cytotoxic brain edema, which contributes to vasogenic edema and ultimately compromises the blood-brain barrier [40,41].

ICP monitoring (ICPM) in patients with ALF is a subject of debate. The use of an invasive ICPM device may increase the risk of intracranial hemorrhage due to the coagulopathy often present in these patients. Conversely, ICPM is essential to avert the adverse effects of increased ICP. ICPM can be performed using either invasive or non-invasive techniques. Invasive ICPM is considered the gold standard, but it is associated with a significant risk of hemorrhage—occurring in 10%–20% of cases and proving fatal in 1%–5%—as well as a risk of infection, which ranges from 0% to 7% in patients with ALF due to their compromised coagulation profiles [42,43]. Noninvasive methods, which include measuring the optic nerve sheath diameter via ultrasonography and employing transcranial Doppler, are available. However, current evidence suggests that these non-invasive techniques do not yield accurate or reliable measurements [44].

The Brain Trauma Foundation guidelines are widely accepted but are specifically tailored to patients with traumatic brain injury. In contrast, there is a notable lack of comprehensive guidelines for ICPM in patients with nontraumatic brain injuries. A recent review of the literature has underscored this gap, pointing out the absence of a uniform consensus on ICPM for patients with ALF [45]. The American Association for the Study of Liver Disease

(AASLD) 2005 guidelines suggest considering ICPM primarily for patients on the transplant list. In the absence of ICPM evidence, these guidelines recommend regular assessments to detect signs of intracranial hypertension and to facilitate the early identification of uncal herniation, assigning an evidence level of III [46]. The AASLD's updated 2011 guidelines introduced the possibility of using recombinant factor rVIIa [47]. The United States Acute Liver Failure Study Group (ALFSG) in 2007 reported insufficient data to endorse routine ICPM for all cases of ALF. Nevertheless, it was noted that many ALFSG members opted for ICPM in patients with advanced (stage III/IV) hepatic encephalopathy [48]. The European Association for the Study of the Liver 2017 guidelines provided a level II-3 evidence and a grade 1 recommendation, advising that ICPM should be considered for a carefully selected subset of patients. This includes those who have progressed to grade 3 or 4 coma, are intubated and ventilated, and have a high risk of intracranial hemorrhage. The guidelines also recommend ICPM for patients presenting with one or more of the following criteria: young age with acute or hyperacute onset; ammonia levels exceeding 150–200 $\mu\text{mol/L}$ that do not respond to initial treatments such as renal replacement therapy and fluids; renal impairment; and the need for vasopressor support [49].

Mendoza Vasquez et al. [45] published an account of their single-center experience with ICPM, utilizing an intraparenchymal modality following coagulation correction guided by viscoelastic testing. Nevertheless, the evidence provided by a single-center study for the use of ICPM is generally not considered robust [45]. To date, there is a lacuna in the available literature regarding the placement of ICPM devices in ALF patients and further studies are needed to establish the use of monitoring modalities in ALF patients.

EARLY EXTUBATION AND ENHANCED RECOVERY AFTER SURGERY

Fast-tracking and early extubation in liver transplant surgery have been associated with improved graft function, reduced hospital stays, and lower overall costs. Currently, nutritional assessment, oral carbohydrate and protein supplementation, and the employment of a portocaval shunt are recommended practices in liver transplantation surgery [50].

Many centers now favor fast-tracking due to its ability to reduce patient discomfort and decrease ventilator-related complications. Factors that support early extubation include transfusion of fewer than five units of PRBCs, a low preoperative Model for End-stage Liver Disease score, reduced inotrope requirements, an optimal graft-to-recipient weight ratio, lower blood lactate levels, and shorter surgical duration [51]. Various studies from different centers, encompassing both adult and pediatric patients with diverse practices, have concluded that early extubation is both safe and cost-effective [52].

CONCLUSION

Perioperative care for liver transplant patients has undergone significant changes over the past few decades due to advancements in surgical and anesthesia techniques. The introduction of new monitoring tools for hemodynamics and coagulation, along with novel pharmacological agents, fluids, and perioperative protocols, has enhanced patient care and expedited recovery. However, there remain some gray areas where perioperative management practices differ among transplant centers, highlighting the need for the development of standardized protocols to ensure uniformity.

ARTICLE INFORMATION

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

ORCID

Saurabh Mittal <https://orcid.org/0000-0002-7056-996X>
 Medha Bhardwaj <https://orcid.org/0009-0001-8634-989X>
 Praveenkumar Shekhrajka

<https://orcid.org/0000-0003-2918-3210>

Vipin Kumar Goyal <https://orcid.org/0000-0002-3318-3726>
 Ganesh Ramaji Nimje

<https://orcid.org/0000-0001-5034-6681>

Sakshi Kanoji <https://orcid.org/0009-0004-2921-8545>
 Suma Katyaeni Danduri

<https://orcid.org/0009-0007-6941-4390>

Anshul Vishnoi <https://orcid.org/0000-0003-4999-730X>

Author Contributions

Conceptualization: SM, VKG. Data curation: MB, PS, GRN. Formal analysis: SK, SKD. Visualization: VKG. Writing—original draft: SM. Writing—review & editing: SM, PS, VKG, GRN, SKD, AV. All authors read and approved the final manuscript.

REFERENCES

1. Fede G, Privitera G, Tomaselli T, Spadaro L, Purrello F. Cardiovascular dysfunction in patients with liver cirrhosis. *Ann Gastroenterol* 2015;28:31-40.
2. Kaur H, Premkumar M. Diagnosis and management of cirrhotic cardiomyopathy. *J Clin Exp Hepatol* 2022;12:186-99.
3. Shin WJ, Kwon HM, Kim SH, Jang HY, Kim JY, Kim JH, et al. Characterizing heart failure with preserved ejection fraction in end-stage liver disease and liver transplant outcomes. *JACC Asia* 2023;3:506-17.
4. Salah HM, Pandey A, Soloveva A, Abdelmalek MF, Diehl AM, Moylan CA, et al. Relationship of nonalcoholic fatty liver disease and heart failure with preserved ejection fraction. *JACC Basic Transl Sci* 2021;6:918-32.
5. VanWagner LB, Lapin B, Levitsky J, Wilkins JT, Abecassis MM, Skaro AI, et al. High early cardiovascular mortality after liver transplantation. *Liver Transpl* 2014;20:1306-16.
6. Głowczyńska R, Galas M, Ołdakowska-Jedynak U, Peller M, Tomaniak M, Raszeja-Wyszomirska J, et al. Pretransplant QT interval: the relationship with severity and etiology of liver disease and prognostic value after liver transplantation. *Ann Transplant* 2018;23:622-30.
7. Harinstein ME, Iyer S, Mathier MA, Flaherty JD, Fontes P, Planinsic RM, et al. Role of baseline echocardiography in the preoperative management of liver transplant candidates. *Am J Cardiol* 2012;110:1852-5.
8. Kwon HM, Moon YJ, Kim KS, Shin WJ, Huh IY, Jun IG, et al. Prognostic value of B-type natriuretic peptide in liver transplant patients: implication in posttransplant mortality. *Hepatology* 2021;74:336-50.
9. Lentine KL, Costa SP, Weir MR, Robb JF, Fleisher LA, Kasiske BL, et al. Cardiac disease evaluation and management among kidney and liver transplantation candidates: a scientific statement from the American

- Heart Association and the American College of Cardiology Foundation. *J Am Coll Cardiol* 2012;60:434-80.
10. Sharma V, Kleb C, Sheth C, Verma BR, Jain V, Sharma R, et al. Cardiac considerations in liver transplantation. *Cleve Clin J Med* 2022;89:46-55.
11. Sussman N, Kaza V, Barshes N, Stribling R, Goss J, O'Mahony C, et al. Successful liver transplantation following medical management of portopulmonary hypertension: a single-center series. *Am J Transplant* 2006;6:2177-82.
12. De Maria S Jr, Nürnberg J, Lin HM, Contreras-Saldivar AG, Levin M, Flax K, et al. Association of intraoperative blood pressure instability with adverse outcomes after liver transplantation. *Minerva Anestesiol* 2013;79:604-16.
13. Mizota T, Hamada M, Matsukawa S, Seo H, Tanaka T, Segawa H. Relationship between intraoperative hypotension and acute kidney injury after living donor liver transplantation: a retrospective analysis. *J Cardiothorac Vasc Anesth* 2017;31:582-9.
14. Smoter P, Nyckowski P, Grat M, Patkowski W, Zieniewicz K, Wronka K, et al. Risk factors of acute renal failure after orthotopic liver transplantation: single-center experience. *Transplant Proc* 2014;46:2786-9.
15. Costa MG, Chiarandini P, Della Rocca G. Hemodynamics during liver transplantation. *Transplant Proc* 2007;39:1871-3.
16. Rocca GD, Costa MG, Feltracco P, Biancofiore G, Begliomini B, Taddei S, et al. Continuous right ventricular end diastolic volume and right ventricular ejection fraction during liver transplantation: a multicenter study. *Liver Transpl* 2008;14:327-32.
17. Biancofiore G, Critchley LA, Lee A, Bindi L, Bisà M, Esposito M, et al. Evaluation of an uncalibrated arterial pulse contour cardiac output monitoring system in cirrhotic patients undergoing liver surgery. *Br J Anaesth* 2009;102:47-54.
18. Krejci V, Vannucci A, Abbas A, Chapman W, Kangra IM. Comparison of calibrated and uncalibrated arterial pressure-based cardiac output monitors during orthotopic liver transplantation. *Liver Transpl* 2010;16:773-82.
19. Su BC, Tsai YF, Cheng CW, Yu HP, Yang MW, Lee WC, et al. Stroke volume variation derived by arterial pulse contour analysis is a good indicator for preload estimation during liver transplantation. *Transplant Proc* 2012;44:429-32.
20. Kim SH, Hwang GS, Kim SO, Kim YK. Is stroke volume variation a useful preload index in liver transplant recipients? A retrospective analysis. *Int J Med Sci* 2013;10:751-7.
21. Dalia AA, Flores A, Chitilian H, Fitzsimons MG. A comprehensive review of transesophageal echocardiography during orthotopic liver transplantation. *J Cardiothorac Vasc Anesth* 2018;32:1815-24.
22. Khurmi N, Seman M, Gaitan B, Young S, Rosenfeld D, Giorgakis E, et al. Nontraditional use of TEE to evaluate hepatic vasculature and guide surgical management in orthotopic liver transplantation. *Case Rep Transplant* 2019;2019:5293069.
23. Pantham G, Waghray N, Einstadter D, Finkelhor RS, Mullen KD. Bleeding risk in patients with esophageal varices undergoing transesophageal echocardiography. *Echocardiography* 2013;30:1152-5.
24. Schroeder RA, Collins BH, Tuttle-Newhall E, Robertson K, Plotkin J, Johnson LB, et al. Intraoperative fluid management during orthotopic liver transplantation. *J Cardiothorac Vasc Anesth* 2004;18:438-41.
25. Feng ZY, Xu X, Zhu SM, Bein B, Zheng SS. Effects of low central venous pressure during preanhepatic phase on blood loss and liver and renal function in liver transplantation. *World J Surg* 2010;34:1864-73.
26. Morkane CM, Sapisochin G, Mukhtar AM, Reyntjens KM, Wagener G, Spiro M, et al. Perioperative fluid management and outcomes in adult deceased donor liver transplantation: systematic review of the literature and expert panel recommendations. *Clin Transplant* 2022;36:e14651.
27. Finfer S, Micallef S, Hammond N, Navarra L, Bellomo R, Billot L, et al. Balanced multielectrolyte solution versus saline in critically ill adults. *N Engl J Med* 2022;386:815-26.
28. Hartmann M, Szalai C, Saner FH. Hemostasis in liver transplantation: pathophysiology, monitoring, and treatment. *World J Gastroenterol* 2016;22:1541-50.
29. Schumacher C, Eismann H, Sieg L, Friedrich L, Scheinichen D, Vondran FW, et al. Use of rotational thromboelastometry in liver transplantation is associated with reduced transfusion requirements. *Exp Clin Transplant* 2019;17:222-30.
30. De Pietri L, Ragusa F, Deleuterio A, Begliomini B, Serra V. Reduced transfusion during OLT by POC coagulation management and TEG functional fibrinogen: a retrospective observational study. *Transplant Direct* 2015;2:e49.

31. Mallett SV. Clinical utility of viscoelastic tests of coagulation (TEG/ROTEM) in patients with liver disease and during liver transplantation. *Semin Thromb Hemost* 2015;41:527-37.
32. Massicotte L, Beaulieu D, Thibeault L, Roy JD, Marleau D, Lapointe R, et al. Coagulation defects do not predict blood product requirements during liver transplantation. *Transplantation* 2008;85:956-62.
33. Massicotte L, Sassine MP, Lenis S, Roy A. Transfusion predictors in liver transplant. *Anesth Analg* 2004;98:1245-51.
34. Goldaracena N, Méndez P, Quiñonez E, Devetach G, Koo L, Jeanes C, et al. Liver transplantation without perioperative transfusions single-center experience showing better early outcome and shorter hospital stay. *J Transplant* 2013;2013:649209.
35. Scott TR, Kronsten VT, Hughes RD, Shawcross DL. Pathophysiology of cerebral oedema in acute liver failure. *World J Gastroenterol* 2013;19:9240-55.
36. Bernal W, Hall C, Karvellas CJ, Auzinger G, Sizer E, Wendon J. Arterial ammonia and clinical risk factors for encephalopathy and intracranial hypertension in acute liver failure. *Hepatology* 2007;46:1844-52.
37. Vaquero J, Chung C, Blei AT. Brain edema in acute liver failure. A window to the pathogenesis of hepatic encephalopathy. *Ann Hepatol* 2003;2:12-22.
38. Rodrigo R, Cauli O, Gomez-Pinedo U, Agusti A, Hernandez-Rabaza V, Garcia-Verdugo JM, et al. Hyperammonemia induces neuroinflammation that contributes to cognitive impairment in rats with hepatic encephalopathy. *Gastroenterology* 2010;139:675-84.
39. Zemtsova I, Görg B, Keitel V, Bidmon HJ, Schrör K, Häussinger D. Microglia activation in hepatic encephalopathy in rats and humans. *Hepatology* 2011;54:204-15.
40. Rai V, Nath K, Saraswat VA, Purwar A, Rathore RK, Gupta RK. Measurement of cytotoxic and interstitial components of cerebral edema in acute hepatic failure by diffusion tensor imaging. *J Magn Reson Imaging* 2008;28:334-41.
41. Kale RA, Gupta RK, Saraswat VA, Hasan KM, Trivedi R, Mishra AM, et al. Demonstration of interstitial cerebral edema with diffusion tensor MR imaging in type C hepatic encephalopathy. *Hepatology* 2006;43:698-706.
42. Raghavan M, Marik PE. Therapy of intracranial hypertension in patients with fulminant hepatic failure. *Neurocrit Care* 2006;4:179-89.
43. Vaquero J, Fontana RJ, Larson AM, Bass NM, Davern TJ, Shakil AO, et al. Complications and use of intracranial pressure monitoring in patients with acute liver failure and severe encephalopathy. *Liver Transpl* 2005;11:1581-9.
44. Rajajee V, Williamson CA, Fontana RJ, Courey AJ, Patil PG. Noninvasive intracranial pressure assessment in acute liver failure. *Neurocrit Care* 2018;29:280-90.
45. Mendoza Vasquez LE, Payne S, Zamper R. Intracranial pressure monitoring in the perioperative period of patients with acute liver failure undergoing orthotopic liver transplantation. *World J Transplant* 2023;13:122-8.
46. Polson J, Lee WM; American Association for the Study of Liver Disease. AASLD position paper: the management of acute liver failure. *Hepatology* 2005;41:1179-97.
47. Lee WM, Stravitz RT, Larson AM. Introduction to the revised American Association for the Study of Liver Diseases Position Paper on acute liver failure 2011. *Hepatology* 2012;55:965-7.
48. Stravitz RT, Kramer AH, Davern T, Shaikh AO, Caldwell SH, Mehta RL, et al. Intensive care of patients with acute liver failure: recommendations of the U.S. Acute Liver Failure Study Group. *Crit Care Med* 2007;35:2498-508.
49. European Association for the Study of the Liver. EASL clinical practical guidelines on the management of acute (fulminant) liver failure. *J Hepatol* 2017;66:1047-81.
50. Brustia R, Monsel A, Skurzak S, Schiffer E, Carrier FM, Patrono D, et al. Guidelines for perioperative care for liver transplantation: enhanced recovery after surgery (ERAS) recommendations. *Transplantation* 2022;106:552-61.
51. Kumar L, Sahu S, Deo AS, Selvakumar R, Panchwag AA, Pavithran P. Recent advances in anaesthesia for abdominal solid organ transplantation. *Indian J Anaesth* 2023;67:32-8.
52. Biancofiore G, Tomescu DR, Mandell MS. Rapid recovery of liver transplantation recipients by implementation of fast-track care steps: what is holding us back? *Semin Cardiothorac Vasc Anesth* 2018;22:191-6.