REVIEW

OPEN

‘Fulminant hepatic failure’ anesthesiologic considerations

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Purpose of review
The aim is to summarize perioperative management of patients with acute liver failure (ALF).

Recent findings
The risk of mortality has decreased due to advancements in supportive care and the admission of ALF patients to the ICU. Noninvasive intracranial pressure monitoring is now preferred over invasive methods. Alternatives like transcranial Doppler have emerged, and treatments such as hypertonic saline and mannitol have proven effective in reducing intracranial hypertension (ICH), a common cause of death in these cases. In contrast, invasive hemodynamic monitoring may be necessary to optimize fluid management and the use of vasopressors or inotropes. Norepinephrine should be the first-choice vasopressor for hemodynamic support. Acute kidney injury frequently occurs in patients with ALF and often necessitates the early initiation of renal replacement therapy (RRT). RRT also helps clear hyperammonemia, which can enhance ICH control. Furthermore, coagulation management should rely on point-of-care viscoelastic tests rather than traditional lab tests, as this provides a more accurate assessment of thrombotic or hemorrhagic risks during ALF.

Summary
Multiorgan failure associated with ALF requires rapid and aggressive treatment to mitigate the risk of fatal outcomes. Key issues that must be effectively managed include encephalopathy, brain edema, severe coagulopathy, hemodynamic instability, and acute kidney injury.

Keywords
acute liver failure, coagulopathy, encephalopathy, hemodynamic monitoring, renal replacement therapy

INTRODUCTION

Acute liver failure (ALF) is defined as having an international normalized ratio (INR) or prothrombin time (PT) greater than 1.5, combined with the onset of hepatic encephalopathy (HE) within 4 weeks of the appearance of symptoms in a patient who does not have pre-existing liver disease [1]. There are some exceptions to this definition, including acute presentations of Wilson’s disease, autoimmune hepatitis, Budd-Chiari syndrome, and hepatitis B virus infection [1,2]. Currently, the term ‘acute liver failure’ is preferred over ‘fulminant hepatic failure’, first introduced in 1970 [3].

Understanding the progression of symptoms is crucial for differentiating among three types of liver failure. The hyperacute form, which includes HE, develops within 7 days of jaundice. The acute form occurs between 8 and 28 days after the onset of jaundice, while the subacute form typically manifests within 5–12 weeks following jaundice [4,5].

In 1999, the International Association for the Study of the Liver introduced slightly different terminology for liver failure (Table 1). They defined ALF as occurring in less than 10 days, fulminant ALF as lasting from 10 to 30 days, and subacute hepatic failure as lasting from 5 to 24 weeks [6].

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KEY POINTS

- ALF incidence is decreasing, but it is associated with high mortality.
- HE with brain edema is the most severe complication.
- Hemodynamic monitoring is necessary to optimize volume status and organ perfusion.
- AKI often requires RRT.
- Multidisciplinary approach is fundamental to manage patients with ALF.

This review aims to: (1) investigate the causes and trends of ALF and (2) discuss effective management and monitoring of ALF patients from an anesthesiology perspective, emphasizing current supportive care practices.

EPIDEMIOLOGY OF ACUTE LIVER FAILURE

Hepatitis A and E infections are major causes of ALF in younger patients, especially in low- and middle-income countries, with mortality rates over 50% [4]. Paracetamol toxicity is the second leading cause in middle-aged individuals in the UK and USA. Drug-induced liver injury is the third most common cause of liver damage, especially in patients over 60 [4,6]. However, the cause of ALF is often unknown, despite extensive investigations [4]. Estimating ALF incidence is challenging, ranging from 1 case per million people annually to about 2000 to 3000 cases in the USA each year [3,4].

CLINICAL COURSE OF ACUTE LIVER FAILURE

The clinical presentation of ALF caused by hepatitis typically shows a time interval from jaundice to encephalopathy that rarely exceeds 7 days [7,8]. Liver injury associated with paracetamol resembles ischemia and occurs rapidly, typically within 8–12 h after consuming an excessive dose [9]. Plasma aminotransferase levels can become significantly elevated while the INR for PT increases, and bilirubin levels usually remain normal or only slightly elevated. These changes typically peak around 72 h after ingestion [10,11▪]. In cases of severe paracetamol overdose, the time between drug ingestion and the initiation of treatment with acetylcysteine is closely linked to patient outcomes [12].

Survival rates for patients diagnosed with ALF have significantly improved in recent years, with mortality rates declining from 85% to approximately 55% thanks to advancements in medical management and treatment protocols [13,14▪,15]. However, timely liver transplantation (LT) is crucial for improving patient outcomes; the 1-year survival rate for these patients is approximately 65–70% [16▪]. Unfavorable outcomes are often linked to serious complications, such as HE, systemic infections, or multiorgan failure [17]. Therefore, comprehensive monitoring and management strategies tailored to the unique needs of each patient are essential, as shown in Fig. 1.

NEUROMONITORING IN ACUTE LIVER FAILURE

Impaired liver function in ALF causes blood ammonia levels to increase [18]. Ammonia is converted in the astrocytes to glutamine, a very active osmotic agent that causes astrocyte swelling, cytotoxic cerebral edema, increased intracranial pressure (ICP), and finally intracranial hypertension (ICH) (ammonia-glutamine hypothesis) [19].

Circulating products resulting from massive liver necrosis are another potential determinant of ICH; toxic products of the failing liver stimulate the production of inflammatory cytokines that increase cerebral blood flow (CBF), disrupting the blood–brain barrier and increasing ICP (toxic liver hypothesis) [20]. This theory is supported by some evidence, which describes how ameliorating refractory ICH provided after urgent hepatectomy can rapidly lower blood toxic products [21].

Table 1. Characteristics of acute liver failure: O'Grady versus Tandon classifications

O'Grady *et al.* [5]	Tandon *et al.* [6]
Hyperacute liver failure: HE within 7 days[a]	Hyperacute ALF: <10 days
ALF: HE between 8 and 28 days	Fulminant ALF: 10–30 days
Subacute LF: HE occurring within 5–12 weeks	Subacute hepatic failure: 5–24 weeks
Disease duration >28 weeks before the onset of encephalopathy is categorized as chronic liver disease	

[a]Considering jaundice as the first symptom.
ALF, acute liver failure; HE, hepatic encephalopathy; LF, liver failure.

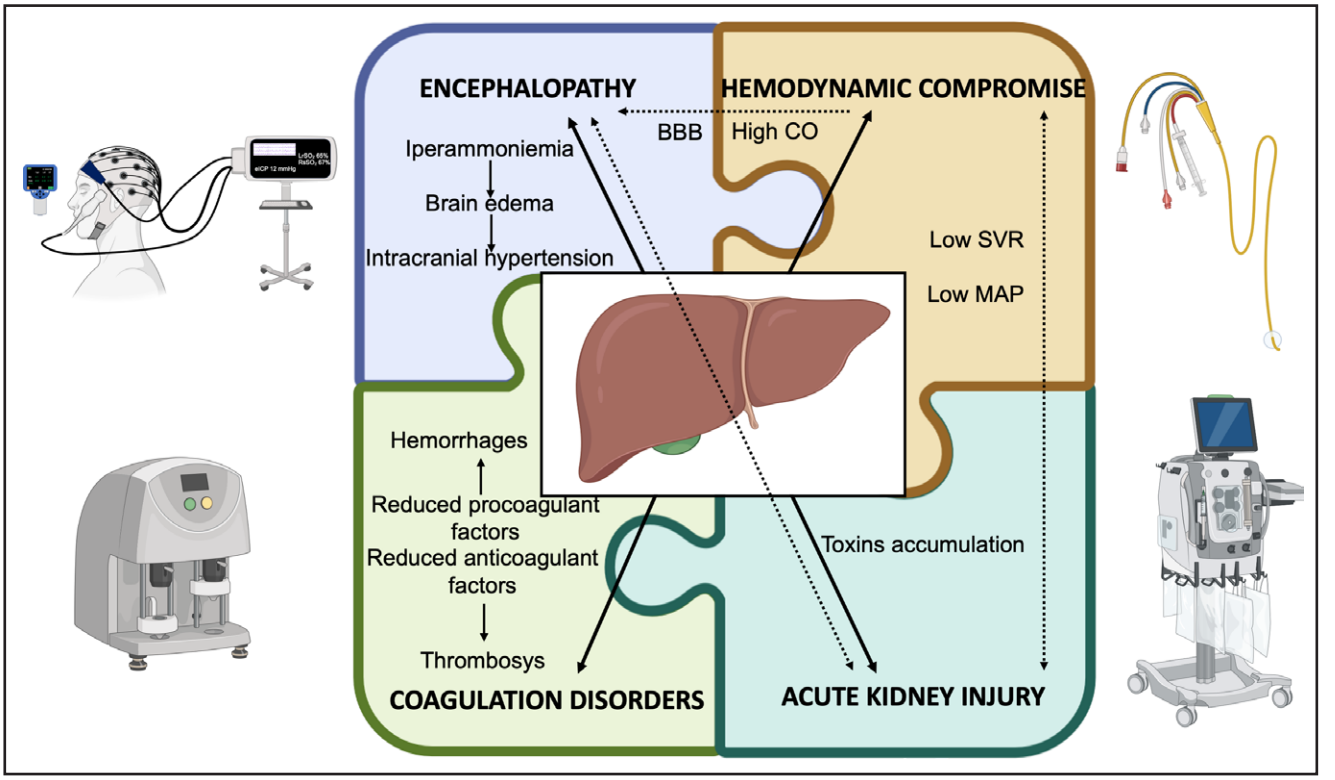

FIGURE 1. Multiorgan approach in acute liver failure patients. Acute liver failure has direct effects (thick arrows) on brain, cardiovascular system, kidneys, and coagulation cascade. Failing organs could have crosstalk (dotted arrows) with other organs, such as kidney–heart crosstalk, brain–heart crosstalk, and kidney–brain crosstalk. Outside the 'puzzle' of multiorgan failure, a multidisciplinary team taking care of these patients should adopt rapid and aggressive countermeasures such as invasive hemodynamic monitoring, renal replacement therapy, multimodal neuromonitoring, and point-of-care viscoelastic tests. BBB, blood–brain barrier; CO, cardiac output; MAP, mean arterial pressure; SVR, systemic vascular resistance.

Therefore, ICH in ALF should be considered multifactorial, with loss of cerebral autoregulation, metabolic changes, release of inflammatory mediators, and ischemic-hypoxic injury being the main drivers [21,22].

The severity of cerebral edema is correlated with the encephalopathy grade, with the most severe intracranial hypertension in grade IV [23]. In extreme cases, brainstem herniation may occur with the death of the patient [24].

Levels of blood ammonia can be used to identify 'high-risk patients': ammonia > 100 μmol/L has a 70% accuracy to predict the development of severe encephalopathy, while levels > 200 μmol/L are strongly associated with the onset of ICH and brain herniation [25▪▪].

For this reason, HE represents one of the main determinants of outcome in these patients, accounting for 30% of total deaths [26].

Clinical evaluation should be focused on an exploration of mental status, including level of consciousness, speech ability, focal neurological deficits, pupil size and light reactivity, posture, and vital signs. However, ICH may be very subtle at the beginning.

Encephalopathy grade III or IV with refractory intracranial hypertension [ICP > 40 mmHg with cerebral perfusion pressure (CPP) < 50 mmHg for more than 2 h] should raise the question of whether or not to transplant the liver, considering the expected poor prognosis [27].

Cerebral hemodynamics changes should also be considered during surgery. There is growing evidence that increased CBF due to hyperdynamic systemic circulation and impaired cerebral autoregulation are of critical importance for the development of brain edema and increased ICP. Moreover, high CBF has been associated with poorer prognosis [28▪].

Contrarily, low cerebral perfusion pressure is associated with hypoperfusion and ischemia.

In an analysis of 116 ALF patients, 11% developed brain death during the perioperative course [29].

Measuring or estimating noninvasively intracranial hypertension is of paramount importance

during perioperative phases of LT in ALF patients to optimize cerebral hemodynamics.

The gold standard method to measure ICP is an invasive probe (either intraparenchymal or intraventricular).

However, ALF-associated coagulopathy poses not negligible risks. Vaquero *et al*. reported intracranial bleeding in 10% among 92 of 332 patients with ALF receiving invasive ICP monitoring [30].

Whereas Rajajee *et al*. demonstrated how a protocol-directed use of invasive ICP monitoring in ALF is feasible, associated with a low incidence of serious complications, and has a significant impact on clinical management [31].

Recent guidelines provided by the Society of Critical Care Medicine do not recommend obtaining invasive ICP considering the risks and given that it has not been demonstrated to improve outcomes [32].

For this reason, and thanks to the development of noninvasive techniques to estimate ICP, bedside tools have become available. Transcranial Doppler (TCD) has been widely used in neurocritical care settings for different purposes such as monitoring CBF, detecting vasospasm or brain death in ICU [33▪▪].

When treating ALF, TCD could be helpful in ruling out ICH (especially referring to TCD estimated CPP), hyperemia, and brain death [34].

The main features of ICH detected with TCD are reduced mean and diastolic flow velocity and increased pulsatility index [PI = (systolic velocity-diastolic velocity)/mean flow velocity] evaluated at the mean cerebral artery [35]. TCD also enables the detection of hyperemic patients characterized by mean flow velocity greater than the reference values using the Lindegaard ratio (mean flow velocity of MCA to mean flow velocity of extracranial internal carotid artery) <3. In this last case, some triggers such as sepsis, hyperthermia, seizures, and anemia should be investigated and eventually treated [36,37].

The worse scenario is brain death as a result of sustained ICH and low CPP lasting hours. In this case, reverberant flow or systolic spikes, evaluated at least twice at 30 min from each other, under normal vital parameters, are highly indicative of cerebral circulatory arrest [38▪].

Another important ultrasound tool available for ICH detection is optic nerve sheath diameter (ONSD) evaluation. The direct communication with the intracranial compartment reflecting increased ONSD (>5 mm) with high ICP (>20 mmHg) makes this method useful and easy to obtain at the bedside or in the operating room (OR) [39▪]. In one ALF pediatric study, none of the survivors had elevated ONSD [40]. However, a more recent study questioned the validity of ONSD in ALF [41]. Some technical aspects should be respected when ONSD measurement is performed [42].

Similarly, automated pupillometry is able to rule out intracranial hypertension and recent evidence supported its use outside ALF [43]. In a 2024 report, in the specific setting of ALF, automated pupillometry demonstrated good anticipation of neuroworsening even when other neuromonitoring tools did not [44]. The main limitation, like ONSD, is the impossibility to perform continuous or semicontinuous monitoring.

For this purpose, besides TCD, there are two monitoring tools available and both are easy to apply at the bedside: near-infrared regional saturation (NIRS) and electroencephalogram (EEG).

NIRS measures regional cerebral oxygen saturation (rSO_2) and analyzes the difference in oxygenated hemoglobin and deoxygenated absorption spectra. Early studies highlighted the potential role of NIRS in detecting changes in CPP during LT [45]. However, some technical aspects should be kept in mind: high total bilirubin or low Hb concentration may induce false low rSO_2 [46]. Even if high levels of bilirubin are not so frequent in ALF, low Hb is frequently seen, therefore raising the suspicion of the 'real' value of low rSO_2.

Finally, cerebral electrical activity, reflecting brain perfusion and metabolism, could be monitored during the perioperative phase thanks to advancements in continuous electroencephalogram (cEEG). Moreover, subtle epileptic activity, such as nonconvulsive status epilepticus, could be detected and treated.

Encephalopathy and intracranial hypertension have a great effect on cEEG, which shows useful prognostic information in ICU [47▪▪].

In the OR during LT, EEG can detect different conditions associated with poor outcomes, such as ischemia, pontine myelinolysis, and cerebrovascular disorders [48,49]. Sometimes, it is difficult to distinguish between anesthetic-related EEG alterations, such as a slowing EEG rhythm, from diffuse ischemic insult.

In conclusion, anesthesiologists nowadays have access to many neuromonitoring tools; however, it is important to recognize the limitations of the data provided. It is advisable to implement site-specific protocols of multimodal neuromonitoring that contemporarily explore CBF, cerebral electrical activity, and intracranial pressure [50].

Whenever ICH is detected, it should be rapidly treated. No significant differences exist in the treatment of ICH between traumatic brain injury and ALF.

Osmotic agents such as mannitol or hypertonic saline are equally effective in reducing ICP. It is

advisable to target plasma sodium 145–155 mEq/L to reduce cerebral edema.

Renal replacement therapy (RRT) could be used to reduce ammonia levels and, therefore, brain edema. For severe refractory ICH, hyperventilation to obtain $paCO_2$ of 30–32 mmHg and moderate hypothermia should be considered.

HEMODYNAMIC MANAGEMENT

From a hemodynamic standpoint, patients with ALF often exhibit hyperdynamic circulation, correlated with liver dysfunction severity. This condition typically presents as distributive shock, with elevated cardiac output (CO) and low systemic vascular resistance [18]. Systemic inflammatory response syndrome contributes to systemic vasodilation. Generally, patients respond well to fluid resuscitation due to preserved cardiac function. Initially, these individuals may experience a mixed shock state that involves both distributive and hypovolemic shock [1–7]. While cardiogenic shock is rare in ALF, it is important to recognize that both macrocirculation and microcirculation are impaired, leading to tissue hypoxia despite adequate arterial oxygenation. Hepatic blood flow increases, especially in the portal circulation, with increased blood flow to the spleen and small intestine, unchanged flow to the colon, and decreased flow to the pancreas and stomach [51,52]. Fluid resuscitation using crystalloids in the early phase is applicable, with normal saline being the most appropriate choice [53]. This is particularly important because patients with ALF often experience hyponatremia. Administering normal saline helps reduce the risk of hypotonicity and lowers the likelihood of cerebral edema. Additionally, many patients with ALF may have a reduced metabolic capacity to process acetate and lactate, which are found in Ringer's solution. The role of albumin as a colloid in ALF has not been thoroughly investigated, it seems to be more relevant as a drug rather than as a resuscitation fluid [53,54]. Patients should receive a blood transfusion when their hemoglobin levels reach the target of 7 g/dl [53–55]. In the second phase, when fluid responsiveness is lost, hepatic blood flow is affected by changes in CO. Makin *et al*. [51] found reduced vascular reactivity in the pulmonary and celiac arteries, with a borderline response in the renal arteries. Lang *et al*. [56] noted that blood flow to the liver and lungs increased, while it remained unchanged in the kidneys and decreased in the hindlimbs. After 12 h, as liver injury progresses and oxygen delivery drops, oxygen consumption declines, resulting in poor outcomes. Venous oxygen saturation (ScvO2), measured through a central venous catheter, serves as an indirect indicator of CO, but its variations are not specific to CO changes [57,58].

Fluid management in these patients should rely on advanced invasive hemodynamic monitoring, such as the pulmonary artery catheter or the less invasive transpulmonary methods [59,60]. Stroke volume variation and pulse pressure variation, as well as CO derived from pulse wave analysis, are often unreliable in this context [61]. Expert use of transthoracic echocardiography or transesophageal echocardiography can provide valuable insights into central hemodynamics [62,63]. It is crucial to maintain an adequate mean arterial pressure (MAP) to ensure proper organ perfusion. If hypotension persists, indicated by a MAP of <60 mmHg despite fluid resuscitation, vasopressor support should be initiated, with norepinephrine being the preferred initial choice. Terlipressin, a commonly used splanchnic vasoconstrictor, has been associated with potentially worsening ICP and is not widely used in cases of ALF [64,65]. In these situations, if the norepinephrine requirement exceeds 0.3 µg/kg/min, it may be advisable to consider adding low-dose vasopressin (1–2 units/h) [66]. This consideration becomes crucial in the later phase (beyond 72 h), as the hepatic artery is the main source of oxygen delivery to the liver. High doses of norepinephrine can have adverse effects, and there is limited data on the effectiveness of vasopressin for reducing liver damage [67].

Patients with ALF in the ICU are at a high risk of developing sepsis. However, identifying septic shock can be challenging. This is particularly true when liver necrosis is present, as the hyperdynamic state associated with this condition can mask the signs of sepsis or septic shock [1–3,68].

LT is crucial for patients with ALF, particularly when ALF does not improve with medical therapy. The King's College Criteria is the most widely used evaluation system and has acceptable specificity, though limited sensitivity [69,70]. In Europe and the USA, patients with ALF receive super-urgent status (status 1) on the transplant waiting list due to their high risk of death within 7 days, prioritizing them over patients with cirrhosis [16▪,71,72].

ACUTE KIDNEY INJURY AND RENAL REPLACEMENT THERAPY

ALF is complicated by acute kidney injury (AKI) in 70% of cases, with 30% of patients needing RRT [73]. Hepatotoxic and nephrotoxic substances, including paracetamol, amatoxin, and sulfonamide

medications, can damage renal tubules [74]. Renal tubular damage can occur concurrently with liver disease and can either resolve or persist. More frequently, patients with ALF from any cause may develop functional renal impairment as part of their circulatory disorders.

During ALF, systemic hemodynamic changes cause renal hypoperfusion and subsequent AKI [75▪▪]. Infections may also evolve into sepsis, contributing to AKI associated with direct bacterial invasion and inflammatory responses [75▪▪].

The brain–kidney crosstalk may contribute to AKI in ALF patients: while electrolyte disturbances, toxic accumulation, and inflammatory cytokines may worsen encephalopathy, brain dysfunction also contributes through cytokine and autonomic nervous system activity to AKI [76]. Some drugs used in the management of ALF, such as certain antibiotics, may also have nephrotoxic effects.

The perioperative management of AKI in a patient with ALF is very complex. Renal function support aims to treat the underlying causes while preventing further renal damage. This includes MAP restoration, optimization of fluid status, electrolyte and metabolic balance, aggressive management of infections, and elimination of nephrotoxic drugs.

Early recognition and intervention can potentially reverse AKI, especially as AKI can affect a patient's suitability for transplantation and adversely affect outcomes and mortality [77]. Therefore, management of these highly complex patients requires a multidisciplinary approach including nephrologists, intensivists, gastroenterologists, and anesthesiologists.

If oliguria persists despite volume repletion and restoration of MAP with vasopressors, early initiation of RRT by continuous renal replacement therapy (CRRT) should be considered [78▪▪]. The kidney disease global outcome guidelines suggest starting RRT in cases of (1) hyperkalemia (>6 mmol/L with electrocardiographic abnormalities); (2) fluid overload/pulmonary edema resistant to diuretic administration; (3) severe metabolic acidosis (pH < 7.15); (4) blood urea concentration greater than 35.7 mmol/L; or (5) stage 3 AKI of renal disease [79]. Guidelines for the management of acute and acute-on-chronic liver failure in adults in the ICU conditionally recommend early initiation of CRRT in patients with ALF, regardless of these conditions [78▪▪]. This approach improves outcomes, particularly in patients affected by rapidly rising serum ammonia levels or otherwise above 150 μmol/L, and established cerebral edema [80].

CRRT is preferable to intermittent hemodialysis because it provides less hemodynamic impact due to greater stability of MAP and renal perfusion. Furthermore, during CRRT, the slow clearance of solutes, especially urea and ammonia, prevents the formation of an osmotic gradient that moves water back into the brain, increasing intracranial hypertension [81]. To the best of our knowledge, no consistent data is available on the optimal timing and thresholds for starting RRT. A case-by-case, careful assessment of the clinical data available must guide physicians in deciding whether and when to start RRT. During liver transplant surgery, continuing or interrupting intraoperative RRT remains a matter of debate largely due to a lack of evidence.

Postoperative AKI occurs in approximately 40.8% of ALF patients undergoing LT, and 7% of them will require CRRT [82]. This complication increases mortality, graft loss, infection, chronic kidney disease, length of ICU, and hospital stay. In a recent meta-analysis, Zhou *et al*. [83] described several modifiable risk factors that showed significant association with AKI after LT (Table 2). Adjuvant hemoadsorbent therapy is a safe, practical, and promising approach to reduce bilirubin and other toxic metabolite levels; however, evidence is lacking [84].

EARLY COAGULATION SUPPORT

In fulminant hepatic failure (FHF), the hemostatic system is altered due to decreased synthesis of procoagulant factors (such as fibrinogen and clotting factors II, V, VII, IX, X, XI, XIII) and a simultaneous decrease in anticoagulant factors, including protein C, protein S, antithrombin, and tissue factor pathway inhibitor [85].

This creates a complex balance between clotting and anticoagulation mechanisms. In addition to these factors, fibrinogen dysfunction, impaired fibrinolysis, platelet dysfunction, and thrombocytopenia resulting from low thrombopoietin levels and platelet sequestration due to portal hypertension-related hypersplenism are also commonly observed in FHF, further complicating bleeding and clotting risk assessments.

The assessment of 'rebalanced hemostasis' has traditionally relied on standard coagulation tests (SCTs), such as PT, activated partial thromboplastin time (aPTT), fibrinogen levels, and platelet count. However, in patients with impaired liver function, SCT abnormalities do not accurately reflect global hemostasis or bleeding risk. Specifically, the American association for the study of the liver and European association for the study of the liver define ALF/FHF by coagulopathy with an INR ≥ 1.5 [1,86], but recent studies emphasize the need for caution when interpreting INR values in relation to hemostasis and bleeding tendencies in FHF.

Table 2. Modifiable factors of acute kidney injury after liver transplantation

Recipient factors	Donor and graft factors
Overweight	DCD organ
Preoperative use of diuretics	Donor BMI > 30 kg/m^2
Preoperative anemia	ABO-Incompatible liver transplantation
	Low graft to recipient body weight ratio
Surgical factors	**Postoperative factors**
Intraoperative hypotension	Postoperative use of vasopressors
Major bleeding	Overexposure to calcineurin inhibitor
Intraoperative use of vasopressors	Calcineurin inhibitor without mycophenolate mofetil
Large intraoperative RBC transfusion	Graft dysfunction
Postreperfusion syndrome	Infection

DCD, donation after cardiac death; RBC, red blood cell.

INR is derived from PT by comparing the patient's PT to a standardized value. Tests like PT and aPTT detect only the reduction in procoagulant factors, meaning INR reflects changes in vitamin K-dependent procoagulants but does not capture deficiencies in anticoagulant factors [87].

Studies show significant inconsistencies in PT/INR results across different laboratories and patient samples, in addition to being a poor predictor of future bleeding events [7], leading to potential inaccuracies in prognosis and clinical decision making [88,89].

Although traditional coagulation tests do not fully capture the complexities of coagulopathy in FHF, viscoelastic tests (VET), such as thromboelastography (TEG) and rotational thromboelastometry (ROTEM), provide a better assessment of the entire coagulation process, including clot formation and degradation.

Devices like Quantra use sonic elasticity estimation, while others (ROTEM, TEG, ClotPro) monitor viscoelastic changes through physical impedance. These instruments provide real-time data on clot formation and lysis, enabling direct visualization of the hemostatic process [90].

Emerging evidence suggests that VET provides a more accurate real-time assessment of coagulation dynamics in FHF [91]. In a prospective study by Seeßle *et al*. [92], ROTEM and SCTs were evaluated in patients with stable liver cirrhosis and ACLF: ACLF patients who experienced bleeding had significantly lower A10 values (across all tests), reduced maximum clot firmness (MCF) in nonactivated thromboelastometry and intrinsic pathway thromboelastometry, and lower fibrinogen levels compared to nonbleeding patients. The study concluded that ROTEM A10 and MCF (similar to MA in TEG) are reliable prognostic markers for bleeding risk in ACLF patients.

Although more reliable than SCTs, an obvious limitation of VET in patients with FHF is that they do not include activation of the anticoagulant protein C system and are insensitive to von Willebrand factor. This is a significant consideration, given that protein C deficiency has been clearly shown to partially correct defects in procoagulant pathways [92], and the highly elevated levels of von Willebrand factor (partially) compensate for thrombocytopenia in liver disease [93].

Thrombin generation assays also provide more accurate assessments by evaluating the interplay between procoagulant and anticoagulant factors, offering a dynamic measurement of thrombin formation, peak levels, and overall coagulation potential.

Three studies have shown that thrombin generation is preserved in patients with ALF, but a particularly hypercoagulable thrombin profile has been observed, identifying the hypofibrinolytic state as a potential risk factor for thrombosis [94–96]. Moreover, although spontaneous bleeding is rare in this specific setting, thrombotic complications are relatively common.

Currently, there are various VET-guided algorithms for clinicians, with differing approaches and transfusion parameters. The greatest discrepancies are observed in bleeding management algorithms, while prophylactic protocols tend to show more consistency. In the latter, transfusion triggers include an R time of 10–15 min, an extrinsic pathway thromboelastometry (EXTEM) clotting time cutoff of 80 s for administering 5–10 mL/kg of fresh frozen plasma, and platelet transfusion based on EXTEM A10 < 40–45 mm and fibrinogen activity thromboelastometry (FIBTEM) A10 > 10 mm or FIBTEM maximum amplitude < 30–32 mm [97,98].

In FHF, the hemostatic system is disrupted. While VET provides better real-time coagulation assessments, no standardized VET-guided protocols exist, highlighting the need for consistent approaches to manage bleeding and transfusion in FHF patients.

CONCLUSIONS

ALF poses great challenges for anesthesiologists and critical care physicians. Multiorgan failure requires rapid and aggressive treatment to reduce fatal outcomes. The main aims include addressing hemodynamic instability and providing adequate perfusion pressure for the brain and other organs. A multidisciplinary team is required to accurately address renal and hemostatic disorders. When patients with ALF are immediately transferred to referral centers with the expertise for treating them, outcomes are significantly improved, and death rates are reduced by nearly 50%. However, considering that ALF is infrequent and most of the available evidence is weak, the authors would welcome a sizeable worldwide effort to create standardized protocols and ameliorate patients' outcomes.

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Conflicts of interest

There are no conflicts of interest.

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