status of the patient (cardiac and inferior vena cava preload assessment, evaluation for hypovolemic vs. vasodilatory vs. cardiogenic shock, left ventricular and right ventricular [RV] function) and may help to guide management.[50]

Ongoing accurate monitoring of hemodynamic and circulatory status must be continued during fluid resuscitation in order to guide appropriate therapy and avoid overresuscitation.[31,51] Monitoring dynamic changes in stroke volume, stroke volume variation, pulse pressure variation, or TTE with fluid boluses or passive leg raise may help guide resuscitation.[52–54] Because of a dearth of ACLF data for cardiovascular complications and shock, it should be acknowledged that a significant amount of data are extrapolated from the general critical care literature.

Resuscitation fluids

Fluid resuscitation i.v. is required for the treatment of hypovolemia and shock states.[55] A meta-analysis of different resuscitation fluids in patients with sepsis and surgical and trauma patients reported that balanced crystalloids (e.g., lactated ringers) and albumin decreased mortality more than hydroxyethyl starch and saline in patients with sepsis.[56] The largest RCT to date (Plasma-Lyte 148 vs. Saline [PLUS] study) found no difference in mortality or AKI in critically ill adults.[55] An updated meta-analysis including this PLUS study (13 RCTs, n = 35,884) concluded that using balanced crystalloids is associated with reduced mortality[57] in the general population of critically ill patients without cirrhosis.

Albumin

Albumin administration is recommended in the management of patients with cirrhosis for select indications (e.g., large-volume paracentesis, paracentesis-induced circulatory dysfunction, spontaneous bacterial peritonitis [SBP], and hepatorenal syndrome [HRS]).[58] Albumin treatment also reduced systemic inflammation and circulatory dysfunction in patients with decompensated cirrhosis.[59] A single-institution, open-label RCT comparing 20% albumin with Plasma-Lyte in 100 patients with cirrhosis and sepsis-induced hypotension reported that albumin had higher rates of shock reversal but no survival benefit and increased pulmonary complications.[60] Another single-institution, open-label RCT (Fluid Resuscitation in Sepsis-Induced Hypotension Among Patients With Cirrhosis study) compared 5% albumin with normal saline in 308 patients with cirrhosis with sepsis-induced hypotension and confirmed that the reversal of hypotension was higher with albumin, with higher 1-week survival (43.5% vs. 38.3%, $p = 0.03$).[61] Unfortunately, there are no large RCT specific to the use of albumin in patients with ACLF. However, recent studies involving albumin in heterogeneous populations may help identify potential adverse events. The Albumin to Prevent Infection in Chronic Liver Failure trial randomized 777 hospitalized patients with decompensated cirrhosis (mostly new or worsening ascites) to daily albumin infusions to maintain serum albumin of 3 g/L throughout the hospitalization or standard care (albumin for large-volume paracentesis, SBP, or HRS).[62] No difference in the composite primary endpoint (infection, renal failure, or death) was identified, and targeting a specific level of albumin may have been associated with significantly higher rates of pulmonary edema and fluid overload. In summary, though albumin has its role in select liver-related indications, its broader use as a resuscitation agent in critically ill patients with cirrhosis and/or ACLF is not well defined.

Vasopressors

Vasopressors may be required for critically ill patients with shock to maintain end-organ perfusion while concurrent fluid resuscitation is ongoing.[63–65] A mean arterial pressure (MAP) target of 65 mm Hg is recommended in septic shock and general ICU patients, but there are no RCTs confirming this approach in patients with cirrhosis or ACLF who generally have lower baseline MAP.[66] A retrospective observational study of 273 critically ill patients with cirrhosis reported that ICU mortality increased below a threshold of 65 mm Hg and suggested maintaining an MAP of >65 mm Hg as an early goal in critically ill patients with cirrhosis.[67] In contrast, a large RCT of general critical care patients with vasodilatory shock (n = 2600) demonstrated that reducing vasopressors with permissive hypotension (MAP target 60–65 mm Hg) was associated with no difference in 90-day mortality (41.0% vs. 43.8%; adjusted OR, 0.82; 95% CI, 0.68–0.98).[67] The optimal approach is to use an individualized MAP target based on frequent assessment of end-organ perfusion (mental status, capillary refill, urine output, extremity perfusion, lactate, central venous oxygen saturation, and end-organ function). Surviving Sepsis Campaign Guidelines suggest invasive arterial monitoring as soon as practical and suggest starting vasopressors peripherally to restore MAP rather than delaying until central venous access is secured.[68]

Norepinephrine (0.01–0.5 μg/kg/min) is recommended as the first-line vasopressor agent to maintain adequate organ perfusion pressure in patients with septic shock.[68,69] Vasopressin deficiency has been documented in cirrhosis as well as in many shock states, and the Surviving Sepsis Campaign Guidelines