Rationale. SBP is a common life threatening complication in cirrhosis (51). Delayed administration of appropriate antimicrobial therapy is associated with increased mortality (38, 39). Third-generation cephalosporins are generally accepted agents of choice for empirical treatment of community acquired SBP (52). However, there is a trend of increased Gram-positive and multidrug resistance pathogen, including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and extended-spectrum beta-lactamase (ESBL) in multiple geographic areas that mandate careful consideration of the initial treatment agent for SBP in settings with high-drug resistance patterns (53, 54). Risk factors associated with Gram-positive and multidrug-resistant SBP are patients with advanced liver disease, severe critical illness, those receiving prophylactic antibiotics and nosocomial or community-acquired SBP (55, 56). A recent systematic review of the literature (nine studies, 520 nosocomial SBP positive ascitic culture) revealed a remarkable high prevalence (30–66%) of multidrug-resistant pathogen, indicating that third-generation cephalosporin may not be viable choices for nosocomial SBP (54). In another systematic review (seven studies, 1,701 participants), third-generation cephalosporin-resistant pathogen were reported in community (33.8%) as well as in nosocomial infections (54.3%), with pooled estimate indicating that nosocomial SBP was associated with a higher risk for resistance compared with community acquired SBP (RR, 1.67; 95% CI, 1.14–2.44; $p = 0.008$) (57). For healthcare-associated SBP, carbapenem-based empirical therapy was associated with lower rate of mortality and treatment failure and more cost effectiveness compared with third-generation cephalosporin-based regimen (6% vs 25%; $p = 0.01$, 18% vs 51%; $p = 0.001$, respectively) (**Supplementary Table 15**, http://links.lww.com/CCM/H302) (58, 59). Thus, we recommend limiting the use of third-generation cephalosporin as the initial empirical treatment to low-risk community-acquired SBP patients in the setting of low prevalence of drug resistance. Active agents against ESBL-producing pathogen (Carbapenems) should be considered for the empirical treatment of healthcare-associated SBP. In high risk critically ill patients and nosocomial infections, tailored approach according to the antimicrobial prevalence pattern covering resistant pathogens (ESBL, MRSA, ± VRE) would be best suited for the empirical therapy. Once culture results are available, antibiotic therapy should be tailored to the narrowest spectrum based on organism sensitivities.

Midodrine and Terlipressin for SBP.

Recommendation. We suggest not using midodrine or terlipressin empirically for critically ill ACLF patients with SBP (Conditional recommendation, very low quality of evidence).

Rationale. SBP is a common infection in ACLF patients. Patients with SBP are at increased risk of developing hepatorenal syndrome. Administration of albumin has been shown to reduce the risk of mortality and renal impairment. Given the underlying vasodilated state, it is possible that administration of vasopressors concomitant with albumin further reduces the risk of renal injury and mortality. Salman et al (60) randomized 200 cirrhotic patients with SBP to one of four groups: albumin, terlipressin, low-dose albumin plus terlipressin, or midodrine. They failed to demonstrate significant differences in mortality or renal impairment in any of the groups. On analysis of the data, we found no differences in the risk of mortality (OR, 1.63; 95% CI, 0.68–3.91), renal failure (OR, 2.63; 95% CI, 0.97–7.17), or resolution of SBP (OR, 0.48; 95% CI, 0.08–52.74) (**Supplementary Table 16*a***, http://links.lww.com/CCM/H302) associated with the use of midodrine in SBP. Two RCTs informed our recommendation regarding Terlipressin. In addition to the above study, Chelarescu et al (61) randomized 55 cirrhotic patients with SBP to cefotaxime or cefotaxime and terlipressin. The cefotaxime and terlipressin group had decreased mortality and increased resolution of SBP at 48 hours and 5 days as well as lower recurrence rates of SBP. On meta-analysis of the data from these two trials, we found no differences in the risk of mortality (OR, 0.66; 95% CI, 0.27–1.58), renal failure (OR, 1.0; 95% CI, 0.32–3.09), or resolution of SBP (OR, 0.86; 95% CI, 0.67–5.15) associated with the use of terlipressin in SBP (**Supplementary Table 16*b***, http://links.lww.com/CCM/H302).

Both studies did not use albumin as standard of care. Furthermore, both studies were at high risk of bias secondary to small sample sizes and lack of concealment, blinding and description of randomization. Further, the study by Chelarescu et al (61) was only published in abstract form.