

Dear ladies and gentlemen, dear ADVOS users and interested parties,

we are pleased to present you another issue of our ADVOS Literature Service. We regularly select one or more papers from international journals which might be of interest to you in connection with our ADVOS procedure. This month we have selected the following:

EXTRACORPOREAL LIVER SUPPORT IN PATIENTS WITH LIVER FAILURE: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED STUDIES.

Alshamsi et al.

Key message

Alshamsi et al. performed a systematic review and meta-analysis of randomized controlled trials examining the efficacy and safety of extracorporeal liver support (ECLS) in patients with liver failure. This study provided evidence that ECLS may improve survival in patients with acute liver failure (ALF) and acute-on-chronic liver failure (ACLF). This effect was more prominent with artificial than with bioartificial devices. The registry data for the ADVOS therapy procedure show exactly the same: the expected survival of the 118 patients was increased by 20%.

Background

The frequency of liver injury and failure in critically ill patients is high. In addition, 60-70% of patients with liver failure suffer from acute kidney injury and about 30-40% need extracorporeal support (Figure 1, adapted from Fuhrmann et al. 2019). ALF is characterized by acute liver injury, hepatic encephalopathy, and an elevated prothrombin time/international normalized ratio (INR > 1.5) in patients without underlying liver disease. Untreated, the prognosis is poor, so timely recognition and management of patients with ALF is crucial. ACLF is a syndrome affecting multiple organs defined by an acute hepatic decompensation in patients with a preexisting chronic liver disease and is normally accompanied by renal dysfunction.

Methods

MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials from inception through March 13, 2019 were searched. Randomized Controlled Trials with adult patients with ALF or ACLF who received either supportive care (control) or supportive care and artificial or bioartificial ECLS were included. Only those describing all-cause mortality or liver-related mortality, bridging to liver transplant, improvement of HE and adverse events were analyzed.

As artificial devices, MARS (Gambro, Lund, Sweden), Biologic-DT (HemoCleanse Inc., USA), FPSA (Prometheus, Fresenius Medical Care Deutschland GmbH, Germany), plasma exchange with hemoperfusion, whole blood exchange and charcoal hemoperfusion were used. Bioartificial modalities included extracorporeal liver assist device (ELAD, Vital Therapies Inc., USA) and HepatAssist (Circe Biomedical Inc., USA).

Results

25 RCTs including 1,796 patients were identified. The average age was 44 years, and 59% of all patients were male. The most common etiologies for ALF were alcohol, viral hepatitis and acetaminophen toxicity. Thirteen RCTs investigated patients with ALF and 13 RCTs with acute-on-chronic liver failure (ACLF). Nineteen trials used artificial ECLS and five trials used bioartificial ECLS. A significant association of ECLS and reduction in mortality (RR 0.84, 95% CI 0.74–0.96, moderate certainty) and significant improvement in hepatic encephalopathy (RR 0.71, 95% CI 0.60–0.84, low certainty) in patients with ALF and ACLF was detected.

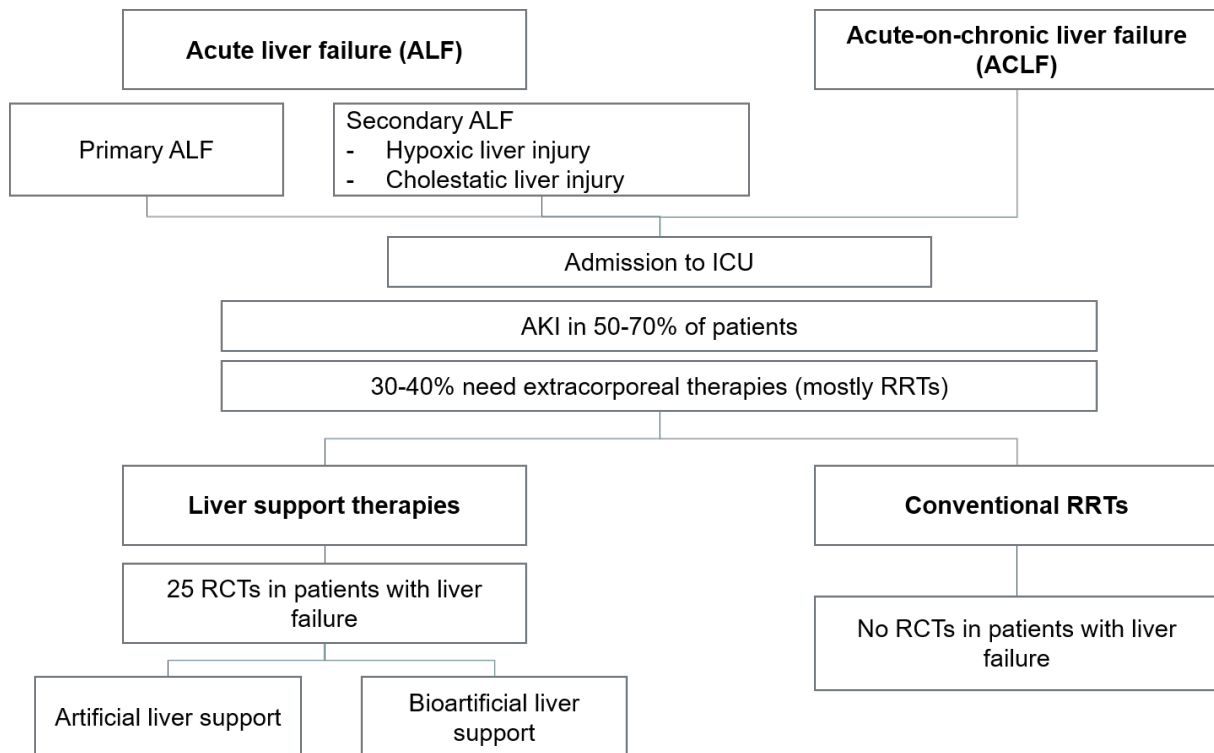


Figure 1: Overview of types of liver failure and extracorporeal therapies. Most frequently, patients suffer from secondary forms of acute liver failure (hypoxic liver injury and cholestatic liver failure, observed in 5–20% of critically ill patients) followed by acute on chronic liver failure (observed in 2–5% of the ICU-population) and primary acute liver failure (< 10 cases per million persons/year).

AKI acute kidney injury, RRT renal replacement therapies, ICU intensive care unit, RCT randomized controlled trial.

Adapted from Fuhrmann et al. 2019: The persistent potential of extracorporeal therapies in liver failure.

The authors conclude:

The meta-analysis showed that ECLS may improve survival and improve HE in patients with liver failure. Before ECLS can be routinely used in practice, future RCTs are needed to determine the significance of effect, the most effective modality, and the subgroup that would benefit the most from ECLS.

We think that:

For the management of liver failure and the initial management of multiorgan failure as bridging device, extracorporeal therapies are of great importance. Alshamsi et al. provided additional proof that ECLS might improve the outcome in patients with ACLF and ALF. Future RCTs are necessary to decide (a) when to start, (b) which treatment modality should be preferred, (c) intensity and (d) duration of extracorporeal therapy. Another recent meta-analysis of pooled individual-patient data of albumin dialysis in patients with ACLF showed that > 4 albumin dialysis sessions significantly improve the survival of patients with ACLF.

These results were observed especially in artificial devices that use albumin dialysis as principle for the therapy. The ADVOS system uses the same. An improvement on expected survival with ADVOS has already been shown in the first report of the EMOS-Registry (DRKS00017068). Its preliminary results have been presented during the DIVI Congress in Hamburg and the complete report will be soon submitted for publication.

If you have further questions or suggestions - please contact us at marketing@advitos.com.