Systematic review and meta-analysis of survival following extracorporeal liver support
Stutchfield BM, Simpson K, Wigmore SJ

CRD summary
The authors concluded that extracorporeal liver support systems appeared to improve survival in acute liver failure but no evidence that they improved survival in acute-on-chronic liver failure. The authors' conclusions reflected the evidence presented but the small number of included studies and limited reporting of quality and review methods should be considered when interpreting the results.

Authors' objectives
To assess the effect of extracorporeal liver support on survival in patients with acute and acute-on-chronic liver failure.

Searching
MEDLINE, EMBASE and Cochrane Central Registry of Randomised Controlled Trials were searched from 1995 to January 2010 for relevant articles; search terms were reported. Reference lists of published articles were scanned.

Study selection
Randomised controlled trials (RCTs) that compared extracorporeal liver support with standard medical therapy for patients with acute or acute-on-chronic liver failure were eligible for inclusion. The primary outcome of interest was all-cause mortality at maximum follow-up. Interventions could include artificial or bioartificial liver support systems. Secondary outcomes included hepatic encephalopathy, biochemical parameters and adverse events.

Most of the studies used artificial extracorporeal liver support with two studies using bioartificial extracorporeal liver support. Treatment regimens varied between studies. Aetiology of acute liver failure was paracetamol overdose, viral hepatitis, anti-TB chemotherapy, acute hypoxic liver failure and fulminant and subfulminant hepatic liver failure. Aetiology of acute on chronic liver failure was cirrhosis and alcoholic liver disease.

The authors did not state how many reviewers selected studies for inclusion.

Assessment of study quality
Study quality was assessed independently by three reviewers using CONSORT criteria and Cochrane Collaboration guidelines. Criteria included randomisation, sequence generation, blinding, sample size calculation and recruitment levels.

Data extraction
Studies were grouped into those with patients with acute liver failure and those with acute-on-chronic liver failure. Data were extracted and used to calculate risk ratios (RRs) and 95% confidence intervals (CIs).

The authors did not state how many reviewers extracted data.

Methods of synthesis
Data were pooled using a random-effects model. The number needed to treat (NNT) was calculated. Heterogeneity was estimated using the Cochran's Q and I². Publication bias was assessed by visual inspection of funnel plots and by the fail-safe N method.

Results of the review
Eight RCTs (355 participants) were included in the review. Randomisation and sequence generation procedures were adequately reported in three RCTs. Details of allocation concealment were reported in five RCTs. None of the included studies were blinded. Two studies provided sample size calculations; sufficient recruitment was achieved in these studies. Follow-up ranged from 27 to 180 days.

Extracorporeal liver support therapy improved survival in acute liver failure (RR 0.70, 95% CI 0.49 to 1.00; three RCTs, I²=0%). The number needed to treat to prevent one death in acute liver failure was eight. There were no...
significant differences for mortality between extracorporeal liver support and standard medical therapy for acute-on-
chronic liver failure (RR 0.87, 95% CI 0.64 to 1.18; five RCTs, I²=35%). There was no evidence of publication bias.

There were also no significant differences for short-term mortality in acute liver failure at seven days (one RCT) or 10
days (three RCTs). There were no significant differences between extracorporeal liver support and standard medical
therapy for adverse events. Results for hepatic encephalopathy, biochemical parameters, adverse events and sensitivity
analysis of case-control studies and excluded RCTs were reported.

Authors' conclusions
Extracorporeal liver support systems appeared to improve survival in acute liver failure but no evidence that they
improved survival in acute-on-chronic liver failure.

CRD commentary
The review question was clear with defined inclusion criteria. Several relevant sources were searched. The authors
assessed publication bias and found no evidence of it but, as they explained, results of the assessment are not always
accurate when only a small set of studies are included. The authors assessed some elements of study quality and
reported some results, although the methods used were unclear. Appropriate methods to reduce reviewer error and bias
were reported for quality assessment; it was unclear whether similar methods were used for study selection and data
extraction. The analysis appeared appropriate.

The authors' conclusions reflected the evidence presented but the small number of included studies and limited
reporting of quality and review methods should be considered when interpreting the results.

Implications of the review for practice and research
Practice: The authors stated that as there was no method to predict waiting time to transplantation in patients with acute
or acute-on-chronic liver failure it seemed appropriate to start all patients who met the criteria for urgent liver
transplantation on extracorporeal liver support therapy where available. In countries where liver transplantation was not
available, extracorporeal liver support therapy may offer the only chance of survival in supporting liver regeneration.

Research: The authors stated that further research was needed to assess efficacy and establish the most appropriate
indications for artificial and bioartificial systems.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.