Extracorporeal liver perfusion as hepatic assist in acute liver failure: a review of world experience

Authors' objectives
To determine the role of allogeneic or xenogeneic extracorporeal liver perfusion (ECLP) for hepatic assist in patients with acute liver failure (ALF).

Searching
The authors conducted searches for reports published in English, German, French, Italian, Spanish, Hungarian, Japanese, Polish and Russian from 1964 to 2000. The sources and search platforms included: NLM Online Databases and Databanks such as MEDLARS and ELHILL (MEDLINE, OLDMEDLINE, HealthSTAR, SERLINE, SERHOLD, DOCLINE, CATLINE, DOCUSER, HISTLINE), PubMed, the Cochrane Library, ISI Web of Science, ISI Current Contents, Internet Grateful Med, CCMed, Index Medicus, DIMDI, and several university libraries in Germany. Additional reports were sought in the reference lists of retrieved publications and through contact with authors. Attempts were made to avoid the duplication of patients reported in multiple sources.

Study selection

Study designs of evaluations included in the review
Information on all patients with ALF undergoing ECLP as hepatic assist were included in the review, regardless of the standard of reporting.

Specific interventions included in the review
Reports of xenogeneic or allogeneic ECLP performed for hepatic assist were included in the review. Reports were only eligible if precise data for ECLP were provided, including perfusion characteristics, donor species, perfusion time and time of discharge. The majority of the patients underwent one or two ECLP applications. The median duration of perfusion was approximately 5 hours. Porcine liver was used in most cases, followed by baboon, human, calf, combination or transgenic donors. Further details were given.

Participants included in the review
Reports of patients requiring hepatic assist for ALF were included in the review. The mean age of the participants was 37.6 years (range: 5 to 79). The majority of the patients were diagnosed with viral hepatitis, followed by drug- or toxin-related ALF, cryptogeneic ALF and alcohol-related ALF. Further details on other causes of ALF were given. The review also included patients with subacute and chronic liver failure.

Outcomes assessed in the review
Reports were eligible if they contained precise data on survival time and cause of death, and if it were possible to allocate clinical follow-up status to one of the following categories: no improvement, neurological improvement, complete recovery, long-term survival, death in ALF, or death from other cause.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Reports of patients were only eligible for inclusion in the review if precise data on methodology and outcomes of patients were provided.

Assessment of study quality
The validity of the included studies was not appropriate in this review, as information on each patient was derived from a synopsis of data reported by centres performing artificial liver support. The validity of the included reports was not applicable to this review.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Data on long-term survival were extracted from each individual patient report and used to derive a survival rate.

Data on age, gender, cause of liver failure, onset of ALF, coma stage, species of donor, technical details of liver perfusion, change in coma stage, time and cause of death, complications during ECLP, and requirement of subsequent liver transplantation were extracted from each individual patient and used to explore the potential impact on prognosis. Details of liver perfusion covered portal versus combined portal/arterial perfusion, perfusion time, use of oxygenator and simultaneous dialysis.

Methods of synthesis
How were the studies combined?
The long-term survival data were presented for the entire dataset and for each of the prognostic groups. A multivariate analysis of variance was performed to explore the impact of prognostic factors, using the general linear method. The results were tabulated and presented in a narrative discussion.

How were differences between studies investigated?
The reports were grouped according to prognostic category. Differences within the groups were assessed using a chi-squared test.

Results of the review
Reports on 270 patients receiving ECLP for acute, subacute or chronic liver failure were identified. Data on 198 patients were included in the analysis.

Overall, the long-term survival rate was 26% in patients undergoing ECLP (n=198) and 21% in those undergoing ECLP using porcine livers (n=140). The authors stated that these did not exceed values reported for conventional intensive care treatment (no data presented).

Prognostic factors associated with improved survival were age younger than 40 years (P<0.029), coma stage lower than III-IV (P<0.003), total perfusion time greater than 10 hours (P<0.024), hepatitis B as the cause of ALF (P<0.05), and the use of human or baboon liver donors (P<0.02).

The use of ECLP as bridging therapy to liver transplantation was successful in 12 out of 14 patients.

Authors' conclusions
The use of porcine livers for ECLP did not better the improvements in long-term survival rate achieved by conventional treatment of ALF.

ECLP using human livers not suitable for liver transplantation may be an effective and practical solution for temporary hepatic support. Bridging to liver transplantation using long-term ECLP has comparable efficacy to bioartifical support methods.

CRD commentary
The review had a clear question. The inclusion criteria appear appropriate given that the intervention is not performed outside of specialist centres or in any clinical trials. The search to identify relevant studies was comprehensive and attempts were made to minimise language and publication bias. The authors did not state whether methods were used to minimise bias in the study selection or data extraction processes. However, the authors restricted inclusion to reports with a clear description of methodology and outcomes.
Details on the characteristics and results of each reported series of patients were given, and the methods used to analyse the data appear to have been appropriate. The authors’ conclusion follows the data presented, although it is not possible to comment on the reliability of the evidence presented for conventional treatment. The authors stated that it is unlikely that a prospective study to assess ECLP in patients with ALF will be performed, and they acknowledge the limitations in the data used in the review. The findings should therefore be viewed with caution, although they are likely to represent the best available evidence in the field.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that the use of ECLP as bridging therapy to liver transplantation needs further evaluation in comparison with other liver support therapies.

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