Living donor liver transplantation in children

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CRD summary
This review evaluated the safety and efficacy of live donor liver transplantation (LDLT) for the treatment of end-stage liver disease in children. The author concluded that the evidence base for LDLT is incomplete, although limited evidence suggests the superiority of LDLT in recipients under the age of 2 years. The conclusion is appropriate based on the evidence presented.

Authors' objectives
To evaluate the safety, efficacy and current status of live donor liver transplantation (LDLT) for the treatment of end-stage liver disease in children.

Searching
The Cochrane Library, CINAHL, EBM Reviews, EMBASE, HealthSTAR, PubMed, the Science Citation Index, Biological Abstracts and the NHS Centre for Reviews and Dissemination's databases were searched from 1995 onwards; the search terms were reported. HTA agencies, research registries, guideline websites and the Internet were also searched. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Systematic reviews or comparator studies with at least 10 participants in each group were eligible for inclusion. Case series reporting data for at least 10 donors were also eligible.

Specific interventions included in the review
Studies of any type of liver transplant where the graft was harvested from a living donor were eligible for inclusion. The comparative graft had to be specifically stated to be eligible. The comparator grafts evaluated in the included studies were cadaveric whole liver transplantation, reduced size liver transplantation (RSLT) and split liver transplantation (SLT). The majority of donors were a parent or a close relative of the child. The most commonly donated liver graft was the left lateral segment. The average age of the donor, where stated, was approximately 30 years (approximate range: 19 to 54 years).

Participants included in the review
Studies of participants aged 18 years or younger who were undergoing liver transplantation for any indication were eligible for inclusion. The median age of the recipients ranged from 0.8 to 11.1 years (approximate age range: 0.3 to 18 years). Studies of patients given another organ transplant at the same time as the liver transplant were excluded. Studies that did not clearly define the age of the transplant recipients were excluded.

Outcomes assessed in the review
Studies that reported at least one of the following outcomes were eligible for inclusion: peri- and post-operative mortality or morbidity, graft survival, convalescence interval, quality of life and liver function.

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

Assessment of study quality
The author did not state that they assessed validity.
Data extraction
The author did not state how the data were extracted for the review, or how many reviewers performed the data selection. Data were extracted on the occurrence of peri- and post-operative safety and efficacy outcomes for donors, and each type of graft for recipients. Where possible, relative risks and absolute risk reduction with 95% confidence intervals were calculated for recipient efficacy and safety outcomes.

Methods of synthesis
How were the studies combined?
The studies were tabulated and combined narratively, grouped by type of graft.

How were differences between studies investigated?
Differences between the studies were assessed by tabulation of the included studies.

Results of the review
Fourteen studies (n=712) evaluated donor outcomes: 1 non-randomised comparative study and 13 case series. Eleven studies evaluated recipient outcomes: 9 non-randomised comparative studies with historical and/or concurrent controls and 2 retrospective analyses of registry data.

Donor outcomes (14 studies).
The mean length of LDLT donor operation ranged from just under 4 to 6 hours, with an average hospital stay of 5 to 14 days. Few donors needed a blood transfusion, and the most common complications were bile leakage (0 to 10%), incisional hernia (2 to 6%), gastroduodenal ulcers (1 to 6%) and wound infection (2 to 6%). The mortality rate for live donors was 0.15%, while approximately 4% of donors required another operation because of LDLT-related complications.

Recipient outcomes.

Cadaveric whole liver transplantation versus LDLT (8 studies).

Cadaveric whole liver transplantation and LDLT were found to have similar overall rates of graft and patient survival: median 5-year survival for patients was 92% with LDLT versus 81% with cadaveric; median 5-year survival for grafts was 81% with LDLT versus 73% for cadaveric transplantation. No clear benefit was found between graft types in terms of vascular complications, bile leakage, reoperation, or graft dysfunction.

An analysis of registry data suggested that LDLT was associated with lower mortality and graft failure rates than cadaveric graft in children younger than 2 years, whereas cadaveric whole graft transplantation was associated with lower rates of mortality and graft failure in children aged 2 to 16 years. LDLT was more likely to be done as an elective procedure in patients with a stable medical state undergoing their first transplant. RSLT versus LDLT (5 studies).

LDLT was associated with more favourable graft and survival rates than RSLT at 5 years: median 5-year patient survival was 92% with LDLT versus 65% for RSLT; graft survival was 81% with LDLT versus 63% with RSLT. Recipients of RSLT were more likely to experience vascular complications. RSLT grafts experienced a much longer ischaemic time than LDLT grafts. Registry data also showed lower patient and graft survival with RSLT in comparison with LDLT.

SLT versus LDLT (5 studies).

LDLT was associated with more favourable actuarial graft and patient survival rates at one year than SLT. However, no difference was found between the graft types at 5 years. The risk of graft dysfunction, blood loss, biliary and vascular complications, bowel perforation and bleeding from the cut liver surface was similar across both graft types.

Authors' conclusions
The evidence base for LDLT is incomplete. There was limited evidence to suggest that LDLT is superior to all forms of cadaveric liver transplantation in children younger than 2 years. However, safety and efficacy in recipients older than 2 years suggest that LDLT is equivalent or worse than SLT and whole liver cadaveric transplantation.

CRD commentary
The review addressed a clear research question and the inclusion criteria were detailed for the participants, intervention, outcomes and study design. Several sources were searched for relevant published and unpublished studies, thus minimising publication bias. Details of the review process, including how the papers were selected for inclusion and how the data were extracted, were not reported; the possibility of reviewer error and bias could not, therefore, be assessed. Furthermore, the author did not appear to have assessed the quality of the included studies, so it was not possible to determine the validity of the studies on which the conclusions were based. Adequate details on each of the included studies were given and the presentation of results in a narrative was appropriate. The results were based on limited data from non-randomised controlled trials with non-comparable treatment groups, case series and registries. The author appropriately considered these limitations in the available evidence in her conclusions and recommendations.

Implications of the review for practice and research
Practice: The author stated that, despite the limitations, LDLT is a life-saving procedure in some children where alternative options are not available. The programmes performing LDLT must adhere to an extremely high standard of care, which includes standard protocols for peri-operative evaluation of potential donors and post-operative follow-up of donors and recipients. In addition, psychosocial evaluation and support programmes should be considered.

Research: The author did not state any implications for further research, although details of ongoing research were reported in the review.

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