Health-related quality of life after liver transplantation: a meta-analysis
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Authors' objectives
To assess health-related quality of life (HRQL) after orthotopic liver transplantation (OLT).

Searching
MEDLINE and EMBASE from January 1966 to October 1998 were searched. MeSH terms searched for included 'adult' and 'liver transplantation' (further details provided). Bibliographies of received articles and conference proceedings were searched for further citations. Only studies published in English were included in the review.

Study selection
Study designs of evaluations included in the review
Studies which presented pre- and post-transplantation data or compared liver transplant recipients to a control group.

Specific interventions included in the review
Liver transplantation.

Participants included in the review
Adult patients undergoing liver transplantation. The mean age of patients was 45 (sd=6.6) years, 54 (sd=21)% were male. Mean length of time from transplantation was 27.5 (sd=21.6) months.

Outcomes assessed in the review
HRQL measures that included an assessment of one or more of the following domains: physical health, psychological health, social functioning, sexual functioning, ability to perform daily activities, and general well-being. 52 unique scales were used by the 49 included studies, 39 studies used a validated HRQL measure. The most frequently used measures were the Karnofsky Performance Status Scale (KPS) (11 studies), Sickness Impact Profile (SIP) (7 studies), Stait-trait Anxiety Inventory (7 studies), Medical Outcomes Survey Short Form 36 (SF-36) (6 studies), Nottingham Health Profile (NHP) (5 studies), NIDDK Liver Transplantation QOL survey (5 studies), Index of Well-Being (5 studies), European Organisation for Research and Treatment of Cancer QOL Questionnaire (5 studies), and Psychosocial Adjustment to Illness Scale-Self-Rate (5 studies). Sixteen studies used self-developed questionnaires.

How were decisions on the relevance of primary studies made?
One author reviewed all titles and abstracts identified in the search for potentially relevant articles.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Two authors independently abstracted relevant study data including patient characteristics (e.g. age, sex, and indication for transplantation), study design, HRQL instrument used, and the scores on pre and post-transplantation HRQL scales. Disagreements were resolved by repeated review and discussion. Abstracted data were entered into an electronic database (Microsoft Excel).

Methods of synthesis
How were the studies combined?
Studies that used the same HRQL instrument were analysed separately. Individual study effect sizes were calculated from a difference in proportions or means between pre- and post-transplantation groups. Effect sizes were weighted by
the number of subjects in the study and combined using random-effects models to estimate an overall effect size.

A nonparametric sign test was used to combine all studies that presented pre- and post-transplantation data for the same HRQP domain (e.g. daily activities, or sexual functioning). Any study that reported a statistically significant improvement was classified as positive, any study that reported statistically insignificant improvements or statistically significant worsening were classified as non-positive. The ratio of positive studies to all studies in a given domain was calculated.

How were differences between studies investigated?
Tests of homogeneity were performed on all summary effects (test used not stated).

**Results of the review**
Forty-nine studies (n=3,576) were included. Of these, 37 studies compared pre- and post-transplantation HRQL data; 12 of these studies and 19 others compared liver transplant recipients with a control group.

HRQL outcomes reported by more than two studies that presented pre- and post-transplantation:

a. KPS (n=6): percentage change for studies that followed up after 1 year was 31.6% (sd=32.1%), p>=0.05. Percentage change for studies that followed up for longer than 1 year (n=4) was 34% (sd=7.8%), p<0.0001.

b. SIP (n=4): summary effect of transplantation on SIP score was 10.5% (sd=4.3%), p<0.008.

c. NHP (n=5): summary effects for improvement after transplantation for all domains were significant (p<0.001), with the greatest improvements in energy (change=51, sd=8.4, p<0.00001) and sleep (change=39, sd=9, p<0.00001)

Combination by HRQL domain.

The results of the sign test show that a statistically significant number of studies report improvement after transplantation for physical health (p<0.004), sexual functioning (p<0.008), daily activities (p<0.02), general HRQL (p<0.02) and social functioning (p<0.05). The ratio of positive to non-positive studies was not significant for psychological health (p<0.08). The HRQL as combined by the sign tests was mildly sensitive (p<0.05) to mean age at time of transplantation and percentage eligible subjects enrolled, but was insensitive (p>0.05) to gender, underlying liver disease, year of report publication, and number of subjects.

**Authors' conclusions**
The HRQL of the patients was impaired pre-transplantation and improved post-transplantation. Transplant recipients reported large gains in those aspects of QOL most affected by physical health and smaller improvements in areas affected by psychological functioning.

**CRD commentary**
A good review of the area. An adequate literature search was conducted although this may have benefited from searching additional databases, and limiting the review to studies published in English may have resulted in important studies being missed, and the results may be subject to publication bias. Inclusion criteria are clearly presented and individual study details are presented in tables included in the review. No validity assessment was carried out and the validity of the studies was not discussed. The authors do not differentiate between the results of studies which incorporate a control group and those which only compared pre- and post-treatment effects. The authors state that they tested for heterogeneity but results of these tests are not presented and so it is not clear whether it was appropriate to pool the studies. Combining the studies results using the sign test appears appropriate in view of the large number of outcome scales used. The authors conclusions follow from the results presented, however, in view of the limitations discussed above these should be interpreted with some degree of caution.

**Implications of the review for practice and research**
Practice: The authors recommend that transplantation treatment programmes expand the psychological and social support available to patients both before and after transplantation. The authors hope that the results of the review will help transplant teams inform potential recipients about what their QOL after transplantation is likely to be. As patients are accepted onto the transplant list, programmes should particularly emphasise treatment to improve disturbed sleep and low energy. Post-transplantation programmes should provide intensive support emphasising tools for improved social functioning, pain management, and mental health.

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