



CCOHTA

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PRE-ASSESSMENT *Living Donor Liver Transplantation*

Before CCOHTA decides to undertake a health technology assessment, a pre-assessment of the literature is performed. Pre-assessments are based on a limited literature search; they are not extensive, systematic reviews of the literature. They are provided here as a quick guide to important, current assessment information on this topic. Readers are cautioned that the pre-assessments have not been externally peer reviewed.

Introduction

End-stage liver disease can be caused by many underlying diseases, including biliary cirrhosis, alcoholic cirrhosis, drug-induced liver failure, cancer or hepatitis.¹ In many forms of end-stage liver disease, drug treatments become ineffective and liver transplantation is the only option.^{2,3}

Most liver transplants are performed using organs from deceased donors, but there is a perpetual shortage of cadaveric livers and many patients die while waiting for a transplant. The liver, however, has an amazing ability to regenerate and for some patients, receiving a partial liver from a living donor may be an alternative. This procedure was first successfully performed in Australia, in 1990, in a living donor liver transplant (LDLT) from a mother to her child.⁴ Since then, the procedure has been done not only for adult to child transplants (usually involving the smaller left lobe of the adult donor's liver), but also for adult to adult transplants (sometimes involving the removal of part of the larger right lobe of the donor's liver).

Over 1,000 LDLTs have been performed worldwide and several Canadian centres perform this procedure.⁴ Preliminary statistics from the Canadian Institute for Health Information's (CIHI) Canadian Organ Replacement Registry show that eight Canadian centres (three each in Quebec and Ontario and one each in British Columbia and Alberta) have liver transplant programs. The number of LDLTs in Canada increased from one in 1993 (the first year that the procedure was performed here) to 44 in 2002. In comparison, the number of cadaveric liver transplantations in 2002 was 334. As of December 31, 2002, 3,956 Canadians were on the waiting list for an organ transplant and 14% of these were waiting for a liver transplant.⁵ CIHI has estimated that 51 people died while waiting for a liver transplant in 2000 and that the number of patients waiting for liver transplantation has increased by 62% over the previous five years.¹

Research Questions

This topic was raised at the April 2003 meeting of the Canadian Coordinating Office for Health Technology Assessment's (CCOHTA) Devices and Systems Advisory Committee. A summary about the technology was presented at this meeting. In the ensuing discussion, it was concluded that donor safety was the key issue.

The earlier CCOHTA summary explained that living donor liver transplantation will not replace cadaveric liver transplantation, but it may be an option for 10% to 30% of liver transplant candidates. Living donor liver transplantation may offer a shorter waiting period for the recipient, with related improvements in morbidity and mortality.⁶

The consideration of ethical issues, such as the use of unrelated donors, is a concern. The American Society of Transplant Surgeons' position paper on living donor liver transplantation explains that this is the only area of medicine in which a major operation is performed on an individual for whom it is medically unnecessary.⁷ As a recent UK review states, procedures must be established to ensure that donors understand the risks and benefits involved and are not coerced.⁸ Moreover, the risks to the donor should not exceed an acceptable level. The authors conclude that living liver donation should not be introduced into the UK without "public debate and approval."

The importance of maintaining technical skill levels and the restriction of the performance of this procedure to specialized centres of excellence should also be considered.^{4,6}

Assessment Process

A preliminary literature search was run on the main sources for health technology assessment information: PubMed, The Cochrane Library (Issue 3, 2003), the Centre for Reviews and Dissemination (NHS EED, DARE and HTA) and EuroScan databases. Internet searches were made using the Google™ search engine. A recent UK review article provided additional references.⁸ The Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) was contacted for information on their forthcoming assessment of this procedure.

Summary of Findings

Living donor liver transplantation is associated with a risk of morbidity to donors of 40% to 60% and a mortality rate of 0.5% to 1%.⁸ The risk varies depending on the type of procedure. In particular, transplantation involving the smaller left lobe of the donor's liver is associated with less risk than right lobectomy.⁸⁻¹⁰ In 2002, the US National Institutes of Health launched a seven-year study of living donor liver transplantation at 10 centres.¹¹ The study will compare outcomes from LDLTs with those for individuals who received cadaveric liver transplants.

| Type of Report | Reference | Findings |
|-------------------|--|---|
| HTA – in progress | <i>Adult-to-adult live donor liver transplantation: recipient outcomes.</i> Adelaide: Australian Safety and Efficacy Register of New Interventional Procedures – Surgical; [forthcoming]. Available: http://www.surgeons.org/asernip-s/net-s/procedures.htm#transplantation . | <ul style="list-style-type: none"> ASERNIP-S has two assessments underway on this topic, one looking at the evidence on outcomes for donors and the other on those for recipients. |
| HTA | <i>Living donor liver transplantation.</i> Lansdale, PA; Hayes Inc.; 2002. Available for purchase: http://www.hayesinc.com . | <ul style="list-style-type: none"> This report is available for purchase. |



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| <p>HTA – Emerging technology briefing</p> | <p><i>Living donor liver transplantation (LDLT)</i>. Bern: Medical Technology Unit, Federal Social Insurance Office Switzerland; 2001. Available: http://www.publichealth.bham.ac.uk/euroscan/ (<i>Euroscan database - member access only</i>).</p> | <ul style="list-style-type: none"> • This briefing covers the potential patient load, costs and ethical issues involved in living donor liver transplantation in Switzerland. • The European Liver Transplant Association has created a registry for this procedure. |
| <p>HTA</p> | <p>Pons JM. <i>Living donor liver transplant</i> [English summary]. Barcelona: Catalan Agency for Health Technology Assessment and Research; 2001. Available: http://www.aatrm.net/ang/informes/summ/br0206.html.</p> | <ul style="list-style-type: none"> • The teams that perform living donor liver transplantation must agree to systematically collect data on outcomes for donors and recipients, so that future donors can make truly informed decisions. • The introduction of living donor liver transplantation may raise ethical and equity conflicts. These must be resolved without endangering other patients on the waiting list. • Mechanisms to ensure transparency and consensus-based prioritization to ensure equitable access are needed. |
| <p>HTA</p> | <p><i>Morbidity and mortality among adult living donors undergoing right hepatic lobectomy for adult recipients</i>. Rockville (MD): Agency for Healthcare Research and Quality; 2001. Available: upon request from info@ahrq.gov.</p> | <ul style="list-style-type: none"> • This assessment summarizes the evidence on donor outcomes for right lobe liver donation. • Donor complications may arise from preoperative procedures, such as biopsy and angiography. • Long-term donor outcomes are still unknown. • Donor mortality in the US is estimated to be 0.26% (two deaths in 771 donations to adult recipients). Donor morbidity has been reported as ranging from 0% to 67%. |



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| HTA | <p><i>Adult-to-adult living-donor liver transplantation</i> [Windows on medical technology no 49]. Plymouth Meeting (PA): ECRI; 2001. Available for purchase from: http://www.ecri.org.</p> | <ul style="list-style-type: none"> • This report is available for purchase. • ECRI has prepared a 1993 assessment of this technology, a 1994 “Executive Briefing” and a 2003 “Hotline Response.” These are available for purchase from ECRI. |
| Guideline | <p><i>American Society of Transplant Surgeons' position paper on adult-to-adult living donor liver transplantation</i>. Alexandria (VA): American Society of Transplant Surgeons; 2000. Available: http://www.astso.org/positionpaper1.cfm. A 2002 review and update of this position paper is summarized at: http://www.astso.org/livingliverdonorupdated.cfm.</p> | <ul style="list-style-type: none"> • Several advantages are associated with living donor liver transplantation. It is an elective operation; there is time to optimize the recipient's condition pre-transplant; a shorter preservation time is needed for the donor liver; a pre-transplant cross-match between the donor and recipient can be made; and the use of LDLTs will increase the available cadaver livers for other patients on the waiting list. • Guidelines for donor and recipient selection, transplant centre criteria and informed consent are needed (the society's recommendations for each are outlined). • There is insufficient evidence to accurately determine the risk for the donor. • The 2002 review of this guideline concluded that the earlier document is still relevant. |
| Conference | <p>Shiffman L, Brown RS, Olthoff KM, Everson G, Miller C, Siegler M, et al. Living donor liver transplantation: summary of a conference at the National Institutes of Health. <i>Liver Transl</i> 2002;8(2):174-88. Available: http://www.dialog-ethik.ch/ethik/d12.pdf.</p> | <ul style="list-style-type: none"> • This 2000 conference reviewed the scientific, medical and non-medical issues in LDLTs and defined the questions for future research. • About 80% of liver transplant programs in the US perform LDLTs. • The long-term risks to the donor and to the recipient remain unclear. |



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Conclusion

In any assessment of this procedure, consideration must be given to the fact that the risks to donors and the benefits to recipients will vary, depending on the type of liver resection, whether the right or left lobe of the liver is used and whether the recipient is an adult or a child.

Although other agencies have evaluated this technology, there may be a need for an assessment in the Canadian context. It would be important to collect the outcomes for donors and recipients through a national registry, to ensure that guidelines for the procedure are developed and to collect information on the costs. Further discussion with relevant agencies is needed to determine if CCOHTA has a role in collecting and assessing such information. It would be important to involve other stakeholders, such as patients and their families, the provincial ministries of health, Health Canada, the Canadian Organ Replacement Register of the Canadian Institute for Health Information, the Canadian Liver Foundation, The Canadian Association of Transplantation and Canadian liver transplant centres.

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