

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional procedure consultation document

Living-donor liver transplantation: donor safety

Many diseases can damage the liver. If damage is severe enough, a liver transplant may be necessary. Living-donor liver transplantation is the replacement of a diseased liver with part of a healthy liver from a donor (usually a relative or a spouse).

The National Institute for Health and Care Excellence (NICE) is examining living-donor liver transplantation and will publish guidance on its safety and efficacy to the NHS. NICE's Interventional Procedures Advisory Committee has considered the available evidence and the views of specialist advisers, who are consultants with knowledge of the procedure. The Advisory Committee has made provisional recommendations about living-donor liver transplantation.

This document summarises the procedure and sets out the provisional recommendations made by the Advisory Committee. It has been prepared for public consultation. The Advisory Committee particularly welcomes:

- comments on the provisional recommendations
- the identification of factual inaccuracies
- additional relevant evidence, with bibliographic references where possible.

Note that this document is not NICE's formal guidance on this procedure. The recommendations are provisional and may change after consultation.

The process that NICE will follow after the consultation period ends is as follows.

- The Advisory Committee will meet again to consider the original evidence and its provisional recommendations in the light of the comments received during consultation.
- The Advisory Committee will then prepare draft guidance which will be the basis for NICE's guidance on the use of the procedure in the NHS.

For further details, see the [Interventional Procedures Programme process guide](#), which is available from the NICE website.

Through its guidance NICE is committed to promoting race and disability equality, equality between men and women, and to eliminating all forms of discrimination. One of the ways we do this is by trying to involve as wide a range of people and interest groups as possible in the development of our interventional procedures guidance. In particular, we aim to encourage people and organisations from groups who might not normally comment on our guidance to do so.

In order to help us promote equality through our guidance, we should be grateful if you would consider the following question:

Are there any issues that require special attention in light of NICE's duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations between people with a characteristic protected by the equalities legislation and others?

Please note that NICE reserves the right to summarise and edit comments received during consultations or not to publish them at all where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would otherwise be inappropriate.

Closing date for comments: 19 March 2015

Target date for publication of guidance: June 2015

Evidence on the efficacy and safety of living-donor liver transplantation was considered to be adequate to support the use of this procedure for suitable recipients in the original NICE interventional procedure guidance on [living-donor transplantation](#). The evidence at that time suggested that living-donor liver transplantation carried a significant risk of morbidity and a small risk of death for donors. This update reviews only the safety of the procedure for donors.

1 Provisional recommendations

- 1.1 Current evidence on the efficacy and safety of living-donor liver transplantation appears adequate to support the use of this procedure for suitable donors and recipients provided that normal arrangements are in place for clinical governance, consent and audit.

- 1.2 During the consent process clinicians should ensure that donors and recipients undergo thorough physical and psychological screening and monitoring, and have counselling about the morbidity and risks associated with this procedure. They should also be provided with clear written information. In addition, the use of NICE's [information for the public](#) *[[URL to be added at publication]]* is recommended.
- 1.3 Living-donor liver transplantation should only be performed on patients selected using the NHS Blood and Transplant (NHSBT) Organ Donation and Transplantation Liver Advisory Group's [Liver Selection Policy](#) and the British Transplantation Society's [Guidelines for Directed Altruistic Organ Donation](#).
- 1.4 Living-donor liver transplantation should be carried out in specialist centres by a multidisciplinary team.
- 1.5 Clinicians should enter details about all donors and recipients undergoing living-donor liver transplantation into the [NHSBT UK transplant registry](#), and review clinical outcomes locally.

2 Indications and current treatments

- 2.1 Liver transplantation is a treatment option for patients with end-stage liver failure. It may also be indicated in patients with some types of primary liver cancer. End-stage liver failure can be either acute (for example, from poisoning) or chronic (for example, because of advanced cirrhosis due to autoimmune, infectious, metabolic or alcoholic liver disease). In children, the most common cause of end-stage liver failure is congenital biliary atresia.
- 2.2 Deceased donor liver transplantation is the established procedure for patients in need of liver transplantation. Limited availability of

deceased donor transplants led to the development of techniques which increase the number of donors who can benefit from 1 available organ. These include split liver grafts (the larger right lobe is usually grafted into an adult and the left lobe into a child) and reduced (segmental) liver grafts.

2.3 The limited availability of deceased donor livers, even with these techniques, has been the stimulus for living-donor transplantation. Living donors are usually blood relatives, but can also be spouses, partners and, in very rare cases, non-directed altruistic donors (volunteers).

2.4 Living-donor liver transplantation may be an option for patients who are deteriorating clinically while waiting for a deceased donor transplant.

3 The procedure

3.1 Living-donor liver transplantation requires 2 operations: a partial hepatectomy performed on the donor; and a hepatectomy (of the native organ) with orthotopic liver transplantation for the recipient.

3.2 During the donor operation a liver lobe (right or left) or segment is resected, preserving the main vessels of the systemic and portal circulation and the main branches of the biliary tree. It is then transported for transplantation into the recipient. Some surgeons choose to graft the middle hepatic vein with the right lobe.

3.3 Operation on the recipient begins with a hepatectomy. The donor's liver lobe or segment is put in place and the blood vessels and bile ducts are anastomosed.

- 3.4 The size of graft (that is, right or left hepatic lobe, or liver segment) is determined by the body size ratio between donor and recipient. Usually right lobe transplants are suitable for adult recipients, whereas left lobe transplants are used for children, or for adult recipients with a small body size. Liver segment transplants may be used for infants and young children.
- 3.5 The right lobe is generally considered to be a better graft for recipients because it provides a larger volume of liver parenchyma, and because the blood and biliary vessels are larger and therefore easier to anastomose. However, a right hepatectomy is a more complex procedure and may be associated with an increased risk to the donor.

4 Safety

This section describes safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#) *[add URL]*.

- 4.1 Donor mortality was estimated as 0.2% (23/11,553) in a worldwide survey of living-donor liver transplant (LDLT) programmes (71 centres, 11,553 patients). Most deaths (15/23) occurred within 60 days and were related to the surgery. A systematic review of donor outcomes (214 studies) also reported that overall donor mortality was 0.2% (12/6000 procedures, 117 studies). Mortality for donation of a left lobe (n=1, 0.05–0.21%) was lower than for right lobe donation (n=5, 0.23–0.5%). In a matched case-control study of 4111 donors, the risk of early death (within 90 days) among donors was estimated as 1.7 per 1000 donors (95% confidence interval

[CI] 0.7 to 3.5) and did not vary with portion of liver donated ($p=0.8$).

- 4.2 Long-term mortality of live liver donors was comparable to that of live kidney donors and National Health and Nutrition Examination Survey participants (1.2%, 1.2% and 1.4% at 11 years respectively, $p=0.9$) over a mean follow-up of 7.6 years in a matched case-control study of 4111 donors.
- 4.3 Donor morbidity of 26% (325/1262) at a median follow-up of 36.5 months was reported in a retrospective case series of 1262 patients. Short-term complications (within 4 weeks of surgery) occurred in 24% (308/1262) of donors. Medium (4 weeks to 3 months) and long-term (after 3 months) complications were rare and occurred in only 2% (17/1262) of donors. Complications were significantly more common in right lobe donors than in left lobe donors (44% compared with 19%, $p<0.05$). The severity of complications was worse in right lobe donors than in left lobe donors.
- 4.4 Severe life-threatening complications were reported in 0.06% (2/3565) of donors (1 had multi-organ failure, 1 had lower body paralysis) in a survey of living donors in 38 Japanese LDLT centres.
- 4.5 The incidence of near-miss events (defined as an event or events with potentially fatal consequences that are successfully managed with no lasting ill-effects) in donors was 1% (126/11,553) in the worldwide survey of LDLT programmes: these events were more frequent at low (less than 50 LDLTs) and moderate volume (51–200 LDLTs) centres compared with high volume centres (more than 200 LDLTs, $p<0.001$).

- 4.6 Transplantation was needed in 0.04% of donors (5/11,553) after liver donation in the worldwide survey of LDLT programmes. Four donors needed liver transplantation because of hepatic failure related to hepatic vein thrombosis and 1 needed kidney transplantation because of nephropathy. Despite transplantation, 2 of these donors died.
- 4.7 Biliary complications were the most common complications reported in both right lobe and left lobe donors in the retrospective case series of 1262 patients at a median follow-up of 36.5 months. The frequency of complications was significantly higher in right lobe donors than in left lobe donors (12% [61/500] versus 5% [38/762], $p < 0.05$).
- 4.8 Infections occurred at a median rate of 6% (range 0–29%, based on 50 studies) in the systematic review of donor outcomes (214 studies). These were most commonly wound infections, urinary tract infections and pneumonia.
- 4.9 Liver dysfunction (needing admission to an intensive care unit) was reported in 3 donors in the survey of living donors ($n = 3565$) in 38 Japanese LDLT centres. Hyperbilirubinaemia was reported in 3% (43/1508) of right lobe liver donors in a multicentre survey of 1508 LDLT donors.
- 4.10 Gastric outlet obstruction was reported in 0.8% (27/3565) of donors in the survey of living donors in 38 Japanese LDLT centres. Small bowel obstruction was reported in 2% (28/1262) of donors (13 in right lobe donors and 15 in left lobe donors) in the retrospective case series of 1262 patients at a median follow-up of 36.5 months.
- 4.11 Intra-abdominal fluid collection was reported in 4% (53/1262) and massive ascites in 0.5% (6/1262) of donors in the retrospective

case series of 1262 patients at a median follow-up of 36.5 months. The incidence was significantly higher in right lobe donors than in left lobe donors (fluid collection: 9.2% versus 0.9%, $p < 0.05$; ascites, $p < 0.05$).

- 4.12 Massive intraoperative bleeding (secondary to clamp failure) and haemorrhage (needing surgical intervention) were reported in 0.3% (39 and 5 out of 11,553 donors respectively) in the worldwide survey of LDLT programmes.
- 4.13 Intra-abdominal bleeding ($n=3$) and bleeding duodenal ulcers ($n=3$) were reported in 0.2% of right lobe liver donors, in the multicentre survey of 1508 LDLT donors.
- 4.14 Pancreatitis occurred in 0.2% ($n=3$) of right lobe liver donors in the multicentre survey of 1508 LDLT donors. Hyperamylasaemia (more than 300 IU/litre) was reported in 0.4% (5/1262) of donors in the retrospective case series of 1262 patients at a median follow-up of 36.5 months. The incidence was significantly higher in right lobe donors than in left lobe donors ($p < 0.05$).
- 4.15 Gastric complications (including gastric volvulus in 2 donors and perforated gastric ulcer in 1 donor) were reported in the worldwide survey of LDLT programmes. Gastric perforation occurred in 1 right lobe liver donor in the multicentre survey of 1508 LDLT donors.
- 4.16 Thrombotic events (including portal vein, inferior vena cava or hepatic vein thrombosis and pulmonary embolism) were reported in 0.2% (24/11,553) donors in the worldwide survey of LDLT programmes.
- 4.17 Cardiac complications (including cardiac arrest and endocarditis in 1 donor each and myocardial infarction in 3 donors) were reported

in the worldwide survey of LDLT programmes. Cardiac failure was reported in 1 donor in the survey of living donors (n=3565) in 38 Japanese LDLT centres.

- 4.18 Gastro-oesophageal reflux due to left liver hypertrophy was reported in 9% (7/83) of adult live-liver donors who had right hepatectomy in a case series of 83 donors at a median follow-up of 69 months.
- 4.19 Aborted hepatectomy was estimated to have occurred in 1% (136/11,553) of procedures on donors in the worldwide survey of LDLT programmes. Most of these aborted hepatectomies (72%, 98/136) occurred before bile duct transection. Aborted procedures were also reported after hepatic transection (n=12) and after anaesthesia but before the incision (n=8). The majority (78%, 106/136) of aborted hepatectomies were 'donor related' and the most common reasons were unexpected vascular or biliary anatomy (n=44), unexpected pathology (n=20), fatty liver (n=14) and haemodynamic instability (n=10). After aborted hepatectomy, 45% (61/136) of donors eventually donated at a second procedure. The incidence of aborted hepatectomy significantly decreased with centre experience ($p < 0.001$).
- 4.20 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers listed the following anecdotal adverse events in donors: prolonged and intractable bile leakage in donors needing repeated interventions, unusual infections (gas gangrene of the stomach) and wound pain. They considered that the following were theoretical adverse events

in donors: donor remnant liver insufficiency, medical or psychological problems and stress related to donation.

5 Committee comments

- 5.1 The Committee was advised that clinical follow-up of donors is desirable and that this should include attention to their psychological wellbeing.
- 5.2 The Committee was advised that there were concerns about patients being selected for living-donor liver transplantation without the NHS Blood and Transplant (NHSBT) Organ Donation and Transplantation Liver Advisory Group's [Liver Selection Policy](#) and the British Transplantation Society's [Guidelines](#) being taken into account. This is underpinned by recommendation 1.3 of this guidance update.
- 5.3 The Committee encourages the [NHSBT UK transplant registry](#) to collect and publish long-term data on donors.
- 5.4 The Committee noted that techniques for living-donor liver transplantation have evolved over recent years and continue to do so.

6 Further information

- 6.1 For related NICE guidance, see the [NICE website](#).
- 6.2 This guidance is a partial review of the NICE interventional procedure guidance on [living-donor liver transplantation](#). This guidance only reviews the safety of the procedure in living donors.
- 6.3 Living-donor liver transplantation is regulated by the [Human Tissue Authority](#).

- 6.4 The NHS Blood and Transplant (NHSBT) Organ Donation and Transplantation Liver Advisory Group are developing a living-donor liver transplantation strategy [URL to be added when available].

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