NICE National Institute for Health and Care Excellence

NICE guidance

Living-donor liver transplantation

HealthTech guidance
Published: 25 November 2015

www.nice.org.uk/guidance/htg390

Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

This guidance replaces IPG194 and IPG535.

1 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 with normal arrangements for clinical governance, consent and audit, provided that the necessary regulatory requirements are followed.

1.2 Clinicians and centres doing this procedure must follow the relevant regulatory and legal requirements of the Human Tissue Authority. This includes carrying out independent assessment interviews and getting statutory approval from the Human Tissue Authority before donation can proceed. During the consent process donors and recipients should have thorough physical and psychological screening and monitoring, and counselling about the morbidity and risks associated with this procedure. They should also be provided with clear written information, including relevant information provided by the Human Tissue Authority. In addition, the use of the information for the public is recommended.

1.3 Living-donor liver transplantation should only be done in accordance with 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, taking into account the legal framework for living donation from the Human Tissue Authority. Non-directed altruistic donation is a possibility and should be discussed with a transplant centre or team.

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 having 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 needing liver transplantation. Limited availability of deceased donor livers led to the development of techniques which increase the number of recipients 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. Some surgeons choose to resect the middle hepatic vein with the right lobe. The liver lobe or segment is then transported for transplantation into the recipient.

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 or by estimating the standard liver volume of both the 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 Efficacy

This section describes efficacy 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.

Recipient outcomes (evidence reviewed in 2006)

A significant amount of literature exists on living-donor liver transplantation both for child and adult recipients, with a number of comparative studies and many case series studies.

4.1 In a review of primary studies assessing outcomes following adult-to-child liver transplantation, median 5-year survival was generally higher in the living-donor group (92%) than in the cadaveric-graft group (81%; based on 8 studies looking at 1,091 living grafts and 4,550 whole-organ cadaveric grafts). Graft survival was also higher with living-donor grafts: the median 5-year survival rate was 81% in the living-donor group, compared with 73% in the cadaveric-graft group.

4.2 The evidence for efficacy in adult-to-adult transplantation was based on a systematic review (246 studies, including 9 comparative studies totalling 675 patients) and a large case-control study (n=2,234). No significant differences in recipient survival at 12 months were found in 3 comparative studies included in the review (80% to 100% in the living-donor group and 75% to 90% in the cadaveric-graft group). In 65 non-comparative studies included in the review, recipient survival rates ranged from 43% to 100% at follow-up of 1 to 36 months.

4.3 Graft survival was also reported in 3 comparative studies. At follow-up of at least 12 months, graft survival was 75% to 89% in the living-donor groups, compared with 73% to 89% in the cadaveric-graft groups.

Donor outcomes (evidence reviewed in 2015)

4.4 A systematic review of living-donor liver transplantation (LDLT) on adult donor outcomes (n=214 studies) reported that nearly all donors had returned to normal

activity by 3 to 6 months (based on 18 studies).

4.5 A systematic review of 11 studies comparing outcomes after right lobe LDLT with or without the middle hepatic vein (MHV) reported no significant differences between the right lobe with MHV versus the right lobe without MHV groups for liver functional recovery. This was based on postoperative peak values of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and total bilirubin (TB) in donors (p=0.08; pooled weighted mean difference -2.88, 95% confidence interval [CI] -6.11 to 0.36). Subgroup analysis showed no difference between the groups for the peak value of ALT (p=0.60), AST (p=0.67) or TB (p=0.06).

4.6 The systematic review of LDLT on donor outcomes (n=214 studies) reported that the non-transplanted part of the donor livers had regenerated to about double the size of their remnant liver within several months, reaching a median of 89% of their original size (follow-up 7 days to 6 months, based on 16 studies).

4.7 A survey of living donors (n=3,565) in 38 Japanese LDLT centres reported liver dysfunction in 3 donors needing admission to an intensive care unit. A case series (survey) of 1,508 LDLT donors reported hyperbilirubinaemia in 3% (43 of 1,508) of right lobe liver donors.

4.8 A case series of 997 donors assessed the long-term health-related quality of life of donors using the SF-36 health survey. Of 578 respondents (58%), the scores for donors were better than the Japanese norm scores (scores more than 50) across all time periods (1990 to 2004). The scores were similar for left lobe (n=367) and right lobe donors (n=211).

4.9 The majority of specialist advisers noted that living-donor liver transplantation is an established procedure in end-stage liver disease, particularly in children. However, there are still some uncertainties about long-term survival and graft function in comparison with cadaveric-liver grafts. For donors, the specialist advisers listed efficacy outcomes as survival, recovery and performance status and psychological wellbeing.

5 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.

Recipient outcomes (children and adults; evidence reviewed in 2006)

5.1 Biliary complications (leaks and strictures) were the most commonly reported complications following living-donor liver transplantation. This was true for both adult-to-child and adult-to-adult transplantation. In a review of literature assessing outcomes following adult-to-child transplantation, the incidence of biliary complications ranged from 5% to 14% (based on 4 studies). Higher rates of biliary complications were reported in 3 case series ranging from 14% (7 of 51) to 34% (14 of 41). Other complications reported included portal vein and hepatic artery thrombosis.

5.2 In a systematic review of adult recipient outcomes, the median reported biliary complication rate was 22.2% (based on 75 studies). Other common complications included infection, and hepatic and vascular complications, with median reported rates of 18.8%, 20.5%, and 7.1%, respectively. In a case series of 259 patients with long-term follow-up, cumulative 1-, 3- and 5-year biliary complication rates were 12.9%, 18.2% and 20.2%, respectively. In this study the majority of patients had undergone right liver grafts.

Donor outcomes (evidence reviewed in 2015)

5.3 Donor mortality was 0.2% (23 of 11,553) in a worldwide survey of living-donor liver transplant (LDLT) programmes (71 centres, 11,553 patients). Most deaths (15 of 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% (13 of 6,000 procedures, 117 studies). Mortality for donation of a left

lobe ranged from 0.05% to 0.21% and was lower than for right lobe donation (0.23% to 0.5%). In a matched case-control study of 4,111 donors, the risk of early death (within 90 days) among donors was estimated as 1.7 per 1,000 donors (95% confidence interval [CI] 0.7 to 3.5) and did not vary with portion of liver donated (p=0.8).

5.4 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 the matched case-control study of 4,111 donors.

5.5 Donor morbidity of 26% (325 of 1,262) at a median follow-up of 36.5 months was reported in a retrospective case series of 1,262 patients. Short-term complications (within 4 weeks of surgery) occurred in 24% (308 of 1,262) of donors. Medium- (4 weeks to 3 months) and long-term (after 3 months) complications were rare and occurred in only 1.5% (17 of 1,262) 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.

5.6 Severe life-threatening complications were reported in 0.06% (2 of 3,565) of donors (1 had multi-organ failure, 1 had lower body paralysis) in a survey of living donors in 38 Japanese LDLT centres.

5.7 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 of 11,553) in the worldwide survey of LDLT programmes: these events were more frequent at low (less than 50 LDLTs) and moderate volume (51 to 200 LDLTs) centres compared with high volume centres (more than 200 LDLTs, p<0.001).

5.8 Transplantation was needed in 0.04% of donors (5 of 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.

5.9 Biliary complications were the most common complications reported in both right lobe and left lobe donors in the retrospective case series of 1,262 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 of 500] versus 5% [38 of 762], p<0.05).

5.10 Infections occurred at a median rate of 6% (range 0% to 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.

5.11 Liver dysfunction (needing admission to an intensive care unit) was reported in 0.08% (3 of 3,565) of donors in the survey of living donors in 38 Japanese LDLT centres. Hyperbilirubinaemia was reported in 3% (43 of 1,508) of right lobe liver donors in a multicentre survey of 1,508 LDLT donors.

5.12 Gastric outlet obstruction was reported in 0.8% (27 of 3,565) of donors in the survey of living donors in 38 Japanese LDLT centres. Small bowel obstruction was reported in 2% (28 of 1,262) of donors (13 in right lobe donors and 15 in left lobe donors) in the retrospective case series of 1,262 patients at a median follow-up of 36.5 months.

5.13 Intra-abdominal fluid collection was reported in 4% (53 of 1,262) of donors and massive ascites was reported in 0.5% (6 of 1,262) of donors in the retrospective case series of 1,262 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: 1.0% versus 0.1%, p<0.05).

5.14 Massive intraoperative bleeding (secondary to clamp failure) and haemorrhage (needing surgical intervention) were reported in 0.4% of donors (39 and 5 out of 11,553 donors respectively) in the worldwide survey of LDLT programmes.

5.15 Intra-abdominal bleeding (n=3) and bleeding duodenal ulcers (n=3) were reported in 0.3% (6 of 1,508) of right lobe liver donors, in the multicentre survey of 1,508 LDLT donors.

5.16 Pancreatitis occurred in 0.2% (3 of 1,508) of right lobe liver donors in the multicentre survey of 1,508 LDLT donors. Hyperamylasaemia (more than 300 IU/

litre) was reported in 0.4% (5 of 1,262) of donors in the retrospective case series of 1,262 patients at a median follow-up of 36.5 months. The incidence was significantly higher in right lobe donors than in left lobe donors ($p<0.05$).

5.17 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 1,508 LDLT donors.

5.18 Thrombotic events (including portal vein, inferior vena cava or hepatic vein thrombosis and pulmonary embolism) were reported in 0.2% (24 of 11,553) of donors in the worldwide survey of LDLT programmes.

5.19 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=3,565) in 38 Japanese LDLT centres.

5.20 Gastro-oesophageal reflux due to left liver hypertrophy was reported in 9% (7 of 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.

5.21 Aborted hepatectomy was estimated to have occurred in 1% (136 of 11,553) of procedures on donors in the worldwide survey of LDLT programmes. Most of these aborted hepatectomies (72%, 98 of 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 of 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 of 136) of donors eventually donated at a second procedure. The incidence of aborted hepatectomy significantly decreased with centre experience ($p<0.001$).

5.22 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.

6 Committee comments

6.1 The committee was advised that clinical follow-up of donors is mandatory and that this should include attention to their psychological wellbeing.

6.2 The committee was advised that there were concerns about patients being selected for living-donor liver transplantation without taking into account the NHS Blood and Transplant (NHSBT) Organ Donation and Transplantation Liver Advisory Group's Liver Selection Policy and the British Transplantation Society's guidelines. This is supported by recommendation 1.3 of this guidance update.

6.3 The committee encourages the NHSBT UK transplant registry to collect and publish long-term data on donors.

6.4 The committee noted that techniques for living-donor liver transplantation have evolved over recent years and continue to do so.

7 Further information

7.1 The Human Tissue Authority has responsibility for approving living-donor transplantation based on criteria set out in the legislation. It also regulates organisations in the UK ensuring they meet the quality and safety standards set out in legislation for the use of human tissue, including organs for living-donor liver transplantation.

7.2 The NHS Blood and Transplant (NHSBT) Organ Donation and Transplantation Liver Advisory Group has developed a living-donor liver transplantation strategy.

Update information

Minor changes after publication

January 2026: Interventional procedures guidance 535 has been migrated to HealthTech guidance 390. The recommendations and accompanying content remain unchanged.

ISBN: 978-1-4731-8231-8

Endorsing organisation

This guidance has been endorsed by Healthcare Improvement Scotland.