NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of living-donor liver transplantation

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).

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This IP overview was prepared in September 2014.

Procedure name

- Living-donor liver transplantation

Specialist societies

- Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland
- British Society of Gastroenterology
- British Transplantation Society
- Royal College of Paediatrics and Child Health

Description

Indications and current treatment

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.

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.

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).

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

What the procedure involves

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.

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. 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.

The size of the 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.

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.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to living-donor liver transplantation. Searches were conducted of the following databases, covering the period from their commencement to 22 September 2014: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Liver donors and recipients.
Intervention/test	Living-donor liver transplantation.
Outcome	Articles were retrieved if the abstract contained information relevant to safety or efficacy: • efficacy - survival, graft survival (recipient) - return to occupation or work (donor) • safety - incidence of complications (recipient) - morbidity and mortality (donor).
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

Evidence reviewed in 2006

NICE guidance on living-donor liver transplantation published in 2006 recommended that current evidence on the efficacy of living-donor liver transplantation and its safety profile appears to support the use of this procedure for suitable recipients. This was based on an overview of evidence, mainly on child and adult recipients. As the 2006 guidance expressed no concerns about efficacy and safety of the procedure for suitable recipients, the evidence base related to recipients has not been updated. It is as follows:"

Evidence on child recipients (table 2)

The evidence on child recipients is based on a heath technology assessment,[1] 2 non-randomised controlled studies[2,4] and a case series[3]. These studies were selected to give an overview of efficacy[1,2], long-term outcomes[3] and specific complications[4].

Evidence on adult recipients (table3)

The evidence on adult recipients is based on a systematic review[5], a non-randomised controlled study[6] and 2 case series[7,8]. These studies were selected to give an overview of efficacy[5–7] and specific complications[8].

The new evidence

Section 1.2 of the guidance published in 2006 suggested that living-donor liver transplantation carries a significant risk of morbidity and a small risk of death to donors. Based on this recommendation, in 2006 the Committee agreed to update the evidence on donor outcomes (specifically morbidity and mortality) in living-donor liver transplantation. The evidence base as it relates to live donors has been updated as follows:

Evidence on donors (table 4)

This is based on an overview of 30,576 patients from 2 systematic reviews[11,16], 6 surveys[9, 12-15 17], 1 matched case-control study[10] and 1 small case series[18]. This figure is an overestimate due to duplicate reporting in systematic reviews and large surveys.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction tables (table 2, 3, 4) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on living-donor liver transplantation (child recipients)

Study 1 Alberta Heritage Foundation for Medical Research (2004)

Details

Study type	**Health technology assessment – review of primary studies**
Country	Canada
Literature search	1995-2004
Study population and number	n= 11 studies (recipient outcomes); Children (< 18 years of age) treated with liver transplantation (any underlying diagnosis) n = 14 studies 712 donors (donor outcomes)
Age and sex	Not reported
Selection criteria	Studies reporting outcomes for at least 10 recipients or donors. Included studies reporting on living-donor liver transplantation, reduced size liver transplantation and split liver transplantation. Both left and right grafts were included.
Technique	CAD whole liver graft, CAD reduced liver graft and CAD split liver graft, LD left lateral segment.
Follow-up	**Up to 12 months**
Conflict of interest/source of funding	None declared

Analysis

Study design issues: This study reported on adult-to-child outcomes. Donor outcomes were also reported.

The CAD transplant group included CAD whole liver graft, CAD reduced liver graft and CAD split liver graft.

Other issues: Not all the reported results comparing CAD subgroups to LD transplants were extracted.

Authors noted that the majority of donors were biologically related, with the left lateral segment the most commonly donated liver graft.

Authors noted that the majority of donor studies did not report the length of follow-up.

Authors noted that the outcomes reported were heterogeneous, and that duplicate publications were also common. Many of the studies provided scant baseline patient information.

Technique and postoperative patient management have changed since some of the earlier studies.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **11 studies (recipient outcomes)** **n = 14 studies 712 donors (donor outcomes)** **Comparative evidence** **Recipient survival** Recipient actuarial survival rates for receiving CAD whole liver and LD liver transplantation were similar for both groups at 6 months. However at a follow-up of between 1 and 5 years, the survival rate was a greater in the LD group (median 5-year survival 92% for LD and 81% for CAD). **Graft survival** Graft actuarial survival rate at 5 years was 81% for LD and 73% for the CAD group. Two studies included in the systematic review reported analyses of data from the Organ Procurement and Transplant Network registry. Both studies found that children under 1 year who had an LD transplant had better outcomes than those who had CAD transplant. Authors noted that children treated with reduced size CAD transplant generally had worse outcomes than those treated with LD transplants. **Donor** The average hospital stay for recipients ranged from 5 to 14 days; the longest hospital stay for a donor was 34 days.	**Recipient:** • 5–14% biliary complications (4 studies) • 7% bowel perforation (1 study) • 9.3% arterial complications (1 study) • 1.9–18.6% hepatic artery thrombosis (3 studies) • 1.9% hepatic artery outflow complications (1 study) • 1.9–27.1% portal vein complications (4 studies) • 1.7% hepatic vein complications (1 study) • 0% venous outflow complications • 7% bleeding. **Donor:** One postoperative death was reported. However, authors state that this person had 3 major risk factors and should not have been accepted as a donor. Most commonly reported postoperative complications were bile leak (0–10%), incisional hernia (6%), gastroduodenal ulcer (1–6%), and wound infection (2–6%). Two studies reported on psychological/quality of life outcomes.
Abbreviations used: CAD, cadaveric; LD, living donor; NR, not reported; NS, not significant (as reported in the study); UNOS, United Network for Organ Sharing.	

Study 2 Reding R (1999)

Details

Study type	**Cohort**
Country	Belgium
Recruitment period	1993-1997
Study population and number	n= 90 child liver transplant recipients 41 related LD; 49 CAD
Age and sex	Mean age: LD group: 1.3 years (range 0.4–13.1 years); CAD group: 1.5 years (range 0.5–15.4 years)
Selection criteria	Indications: 34 (of 41) patients in the LD group and 41 (of 49) patients in the CAD group had biliary atresia. The rest of the patients in both groups had other conditions (not specified).
Technique	CAD: whole donation (n = 20), reduced size liver transplantation (n = 21) and split liver transplantation (n = 8) Related LD group – left liver transplant
Follow-up	**Unclear**
Conflict of interest/source of funding	None declared

Analysis

Study design issues: This study reported on adult-to-child outcomes. Some donor outcomes were reported.

This study was not included in the above systematic review. This is a retrospective comparison.

Original study group had 110 patients. However, there were 11 pretransplant deaths (10 CAD, 1 LD). Nine patients were still on the CAD waiting list.

In the LD group the donor was mostly the mother or the father (n = 39).

Immunosuppression management did not vary between the 2 groups.

LD group – 32 children were included as the preferred transplant option, whereas 9 were initially on the CAD transplant waiting list and underwent LD transplantation because of clinical deterioration.

CAD group – Living donation was not considered in 37 patients; in 12 cases donors were evaluated.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>Number of patients analysed: 90 child liver transplant recipients
41 related LD
49 CAD

Actuarial recipient survival, actuarial graft survival
<table>
<tr><th></th><th>LD</th><th>CAD</th><th>p value</th></tr>
<tr><td>Recipient</td><td></td><td></td><td></td></tr>
<tr><td>1-year survival</td><td>92%</td><td>87%</td><td>NS</td></tr>
<tr><td>2-year survival</td><td>89%</td><td>85%</td><td>NS</td></tr>
<tr><td>Graft</td><td></td><td></td><td></td></tr>
<tr><td>1-year survival</td><td>90%</td><td>75%</td><td>NS</td></tr>
<tr><td>2-year survival</td><td>84%</td><td>75%</td><td>NS</td></tr>
</table>
Donor outcomes: Not reported.</td><td>Complications:

Recipient:

LD group, n = 41
0 patients had hepatic artery thrombosis (p = 0.20).
1 (2%) patient had portal vein thrombosis (p = NS).
0 patients had primary non-function (p NR).
14 (34%) patients had biliary complications (p = 0.044)
• 10 (24%) stenosis
• 3 (7%) leaks
• 1 (2%) other.

CAD group, n = 49
8 (16%) patients had hepatic artery thrombosis.
4 (8%) patients had portal vein thrombosis.
0 patients had primary non-function.
7 (14%) patients had biliary complications
• 6 (12%) stenosis
• 0 leaks
• 1 (2%) other.

Donor:

• 3 donors developed biliary leaks that healed spontaneously.
• 2 patients developed incisional hernias.
• 1 patient developed a pleural effusion.</td></tr>
<tr><td colspan="2">Abbreviations used: CAD, cadaveric; LD, living donor; NR, not reported; NS, not significant (as reported in the study); UNOS, United Network for Organ Sharing.</td></tr>
</table>

Study 3 Reding R (2001)

Details

Study type	**Case series**
Country	Belgium
Recruitment period	1993-1999
Study population and number	n= 77 child liver transplant recipients all LD
Age and sex	Median age at transplant 1.1 years (range 0.4–13.1 years).
Selection criteria	Indications: biliary atresia (n=55), progressive familial intrahepatic cholestasis (n=6), hepatic malignancy (n=5), cholestatic cirrhosis (n=4), fulminant hepatitis (n=2), other (n=5). Prior to transplantation 41 children were at home, 32 were hospitalised and 4 were in the intensive care unit.
Technique	Left lobe hepatectomy was performed in the living donors
Follow-up	**Unclear**
Conflict of interest/source of funding	None declared

Analysis

Study design issues: This study reported on adult-to-child outcomes. Some donor outcomes reported.

Same study group as above – probable that there is overlap of cases and reporting.

In 73 cases, the donor was the mother or the father.

Limited information given on the characteristics of the recipients. However, paper does report long-term rates.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>Number of patients analysed: 77 child liver transplant recipients

Actuarial recipient survival, actuarial graft survival

<table>
<tr><td></td><td>LD</td></tr>
<tr><td>Recipient</td><td></td></tr>
<tr><td>1-year survival</td><td>92%</td></tr>
<tr><td>5-year survival</td><td>89%</td></tr>
<tr><td>Graft</td><td></td></tr>
<tr><td>1-year graft survival</td><td>90%</td></tr>
<tr><td>5-year graft survival</td><td>86%</td></tr>
</table>
Two patients underwent retransplantation for chronic rejection.

Donor outcomes: Not reported.</td><td>Complications:

Recipient:
Causes of death were:
Adenovirus hepatitis
Delayed graft function complicated by portal thrombosis
Recurrent neonatal hepatitis
Recurrent hepatoblastoma
Post-transplant lymphoproliferative syndrome
Recurrent hepatocarcinoma
Biliary sepsis
Unknown etiology.
Morbidity:
8 (10%) portal vein thrombosis
1 (1.2%) hepatic artery thrombosis
14 (18.7%) biliary stenosis.
Donor:
Authors reported that there were no significant intraoperative complications.
1 donor required blood transfusions.
5 donors developed biliary leakage that resolved spontaneously.
3 donors developed hernias.
2 donors developed pleural effusion.
1 donor developed cubital nerve compression.</td></tr>
<tr><td colspan="2">Abbreviations used: LD, living donor; NR, not reported; NS, not significant (as reported in the study); UNOS, United Network for Organ Sharing.</td></tr>
</table>

Study 4 Drews D (1997)

Details

Study type	**Cohort**
Country	Germany
Recruitment period	1991-1996
Study population and number	n= 100 child liver transplant recipients 51 LD; 49 CAD
Age and sex	LD: Mean age: 30 months (range not stated). Mean body weight 11.6 kg (range not stated) CAD: Mean age: 71 months (range 10–17.8 years). Mean body weight 21 kg (range 2.7–58 kg)
Selection criteria	Children undergoing LD transplantation were significant younger and weighed significantly less than children undergoing CAD transplantation ($p < 0.0001$). Indications: Most patients had biliary atresia (n = 47). Other indications included acute hepatic failure, neonatal hepatitis and autoimmune hepatitis UNOS classifications were given 22 LD UNOS 1 and 2; 17 CAD patients UNOS 1 and 2.
Technique	Not stated given the publication date it would assumed the majority would have been left liver grafts
Follow-up	**Not stated**
Conflict of interest/source of funding	Not specified

Analysis

Study design issues: This study reported on adult-to-child outcomes. Donor outcomes were not reported.

Limited efficacy outcomes as the primary aim of this paper was to report complications following liver transplantation.

In general outcomes not described well – and in some outcomes absolute figures were not reported.

Children undergoing LD transplantation were significant younger and weighed significantly less than children undergoing CAD transplantation ($p<0.0001$).

The incidence of acute rejection was different in groups with different body weights.

Other issues: Authors noted that there was a decreased rate of rejection in children below 20 kg, indicating a better graft tolerance in younger children.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **100 child liver transplant recipients** **Actuarial recipient survival, actuarial graft survival** In July 1996, overall patient survival was 78%. Survival in the LD group was 71%; in the CAD group 86% (difference was NS – no p value given). *Mean follow-up was not stated.* Graft survival was 68% (follow-up not stated). **Retransplants** Six patients had 1 retransplant and 5 patients had 2 retransplants (unclear what group). **Donor outcomes**: Not reported.	**Complications** LD group, n=51. • 36 (70.5%) patients had bacterial infections • 72% patients had acute rejection • 1 patient had chronic rejection • (LD group, 90% of acute rejection episodes occurred in the first months after transplantation) • 7 (13.7%) patients had bile leaks • 2 (4%) patients had hepatic artery thrombosis • 6 (11.8%) patients had venous thrombosis. CAD group, n = 49 • 26 (53%) patients had bacterial infections. • 64% acute rejection in the CAD group. • 3 patients had chronic rejection. • CAD group 25% of acute rejection episodes occurred later. • 4 (8%) patients had bile leaks. • 4 (8%) patients had hepatic artery thrombosis. • 5 (10%) patients had venous thrombosis. In terms of bacterial infection the authors noted that there was a significant difference between the groups (p = 0.05). Most infections were sepsis (58%). The incidence of bacterial infection also differed between the UNOS groups. In terms of viral infections there was limited information to provide breakdown – overall rate n = 48/100 **Donor outcomes**: not reported.
Abbreviations used: CAD, cadaveric; LD, living donor; NR, not reported; NS, not significant (as reported in the study); UNOS, United Network for Organ Sharing.	

Table 3 Summary of key efficacy and safety findings on living-donor liver transplantation (adult recipients)

Study 5 Middleton P (2003)

Details

Study type	**Systematic review**
Country	Australia
Literature search	1990-2003
Study population and number	n= 246 studies (including 9 comparative studies)
Age and sex	LD: Mean age: 30 months (range not stated). Mean body weight 11.6 kg (range not stated) CAD: Mean age: 71 months (range 10–17.8 years). Mean body weight 21 kg (range 2.7–58 kg)
Selection criteria	Population: Authors noted that most of the studies were level IV (case series), with some comparative studies of III-2 (concurrent comparisons) or level III-3 (historical comparisons). Indications: All studies using any surgical technique for transplanting a liver from a live adult (> 18 years) donor to an adult or child recipient were included.
Technique	Articles reporting on any surgical live liver technique were included.
Follow-up	**Unclear (maximum follow-up appears to be 24 months)**
Conflict of interest/source of funding	None declared

Analysis

Study design issues: This study reported on adult-to-adult outcomes.

Only recipient outcomes were reported on here as donor outcomes are have been published in a separate paper and are described in detail in table 4.

Comparison of adult and child recipient outcomes were reported in the review but have not been extracted in this table.

Outcomes reported in the review that have not been extracted here include: blood loss and transfusion, 'other' complications, functional grafts rates, reoperation, regeneration, operation time, ICU /hospital stay, waiting time, liver function and quality of life (very limited information).

The most common complications were biliary or hepatic complications or infections.

Other issues: Authors noted that in general the complication rate was higher in the first transplant recipients – suggesting an effect of experience. However, none of the differences were reported as statistically significant.

Percentages should be treated with caution given the small number of cases in many of the studies.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>
Number of patients analysed: 246 studies (including 9 comparative studies)
Recipient survival, graft survival
Comparative evidence (9 studies)
<table>
<tr><th>Survival</th><th>LD</th><th>CAD</th><th>p value</th></tr>
<tr><td>Ham 2001, Follow-up - 12 m</td><td>80%</td><td>90%</td><td>NR</td></tr>
<tr><td>Kosari 2003, Follow-up – 12 m</td><td>100%</td><td>89%</td><td>NS</td></tr>
<tr><td>Liu 2003, Follow-up – NR</td><td>57%</td><td>9%</td><td>< 0.05</td></tr>
<tr><td>Lo 1999, Follow-up – NR</td><td>85%</td><td>80%</td><td>NR</td></tr>
<tr><td>Marcos 2000, Follow-up – NR</td><td>90%</td><td>97%</td><td>NR</td></tr>
<tr><td>Pomposelli 2002, Follow-up – 6 m</td><td>80.1 %</td><td>91.6%</td><td>NS</td></tr>
<tr><td>Testa 2000, Follow-up –12 m</td><td>80%</td><td>75%
80%</td><td>NR</td></tr>
<tr><td>Graft survival</td><td></td><td></td><td></td></tr>
<tr><td>Ham 2001, Follow-up - 12 m</td><td>76%</td><td>88%</td><td>NR</td></tr>
<tr><td>Kosari 2003, Follow-up – 12 m</td><td>89%</td><td>89%</td><td>NR</td></tr>
<tr><td>Marcos 2000, Follow-up - NR</td><td>85%</td><td>92%</td><td>NS</td></tr>
<tr><td>Marcos 2000, Follow-up - NR</td><td>87%</td><td>94%</td><td>NR</td></tr>
<tr><td>Pomposelli 2002, Follow-up - 24 m</td><td>80.1 %</td><td>89.4%</td><td>NR</td></tr>
<tr><td>Testa 2000, Follow-up – 6 m</td><td>75%</td><td>73%</td><td>NR</td></tr>
<tr><td>Trotter 2000, Follow-up – NR</td><td>90%</td><td>90%</td><td>NS</td></tr>
</table>
Non-comparative evidence
Survival
Survival was reported in 65 studies with a follow-up of 30 days to 3 years. Median survival was 85.2%, (range 42.9–100%).
Recipient mortality was reported in 115 studies, with a median reported rate of 12.5% (range 0–50%).
Graft survival
Graft survival was reported in 48 studies with a follow-up of 30 days to 3 years. Median graft survival was 82.6% (range 63.2–100%).
Graft loss was reported in 18 studies, with a median reported rate of 8% (range 0–26.7%).
Retransplantation
Retransplantation rates were given in 38 studies, with a median rate of 9.3% (range 0–100%)
</td><td>
Complications:
Comparative evidence
Authors state that 24 studies compared CAD and LD complications. Biliary complications were seen more often in LD recipients. There were no statistically significant differences reported in other complications, although there seemed to be higher incidence of hepatic artery thrombosis and hepatic vein outflow obstruction in LD compared with CAD. There also appeared to be a greater incidence of rejection in CAD recipients (1 study each).
Non-comparative evidence
20 studies reported overall complication rate. The median reported rate was 44.8%, with the total complication rate ranging from 0% to 100%.
Total average complications per patient were reported in 5 studies, with a median of 0.7 (range 0.4–4.3).
Biliary complications
The median reported rate of biliary complications in LD recipients was 22.2% and ranged from 0% to 100% (75 studies).
Infections
The median reported rate of infection in LD recipients was 18.8% and ranged from 0% to 100% (30 studies).
Vascular complications
The median reported rate in LD recipients was 7.1%, range 0–100% (63 studies).
Hepatic complications
The median reported rate in LD recipients was 20.5%, range 0–100% (30 studies).
</td></tr>
<tr><td colspan="2">Abbreviations used: CAD, cadaveric; LD, living donor; NR, not reported; NS, not significant (as reported in the study); UNOS, United Network for Organ Sharing.</td></tr>
</table>

Study 6 Thuluvath PJ (2004)

Details

Study type	**Case–control.** For each patient treated with LD transplant 2 CAD transplant controls were selected, matched for age, gender, race, diagnosis and year of transplantation
Country	USA
Recruitment period	1988-2001
Study population and number	n= **764 adults LD; 1470 adults CAD (matched controls)**
Age and sex	LD – 49.7 years (range not stated). 43.3% female, CAD – 49.8 years (range not stated). 43.1% female,
Selection criteria	Population: LD: 16.2% hospitalised at the time of transplantation, 4.7% in ICU CAD: 11.5% hospitalised at the time of transplantation, 22% in ICU Indications: LD and CAD: Most common primary diagnosis hepatitis C (32%)
Technique	Not described
Follow-up	**2 years**
Conflict of interest/source of funding	None declared

Analysis

Study design issues: This study reported on adult-to-adult outcomes.

For this study data were used from the UNOS database.

The study compared the outcomes of patients who underwent LD transplantation with a matched group of CAD transplant recipients.

It was not possible to identify matched controls for 29 LD transplant patients.

Age, gender, race, diagnosis and year of transplantation were similar in both groups. Serum creatinine and cold ischaemia time were higher in the CAD group. **There were more patients in the CAD group who were on life support and in ICU and were UNOS status I or 2 – suggesting that the CAD group was considerably sicker than the LD group at time of transplantation**.

The majority of living donors were blood relatives.

Other issues: Authors suggested that early experience may explain the results – given that LD has been performed predominantly since 1999 (no sensitivity analysis was done excluding those who had a transplant prior to 1999).

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **764 adults LD** **1470 adults CAD (matched controls)** **Recipient survival, graft survival** 2-year survival was 79.0% in the LD group compared with 80.7% in the control group (p = 0.5). Authors noted that whereas patient survival was similar, 2-year graft survival was significantly lower in the LD group (64.4% vs 73.3%) p < 0.001 – suggesting that a number of patients underwent retransplantation. Authors noted that after regression analysis (adjusting for confounding variables) patients who had LD transplants were 60% more likely to lose the graft within 2 years (majority in the first year) compared with CAD transplants (hazard ratio 1.6; CI 1.1 to 2.5). Primary graft non-function was reported in 27 (3.5%) of the LD group and 49 (3.3%) of the CAD group.	**Complications**: Authors noted that for the majority of patients (around 90%) complications were not reported by UNOS classification. Of the reported complications, infection was higher in the LD group (25.4% vs 14.3%; p=0.05). Biliary complications were also more common in the LD group (8.5% vs. 4.2%) (NS – although authors noted very small sample size).
Abbreviations used: CAD, cadaveric; LD, living donor; NR, not reported; NS, not significant (as reported in the study); UNOS, United Network for Organ Sharing.	

Study 7 Olthoff KM (2005)

Details

Study type	**Case series**
Country	USA
Recruitment period	1998-2003
Study population and number	n= **385 patients treated with LD liver transplantation**
Age and sex	Mean age was 49 years (range not reported). 59% males.
Selection criteria	Population: 11% of patients were hospitalised at the time of the treatment and 4% were in ICU Indications: The most common diagnosis was hepatitis C cirrhosis (46%), followed by liver disease (18%)
Technique	Right lobe grafts. Mean graft weight was 966 g (range 470–1729 g)
Follow-up	**1 year**
Conflict of interest/source of funding	None specified

Analysis

Study design issues: This study reported on adult-to-adult outcomes.

Data from this study came from the A2ALL retrospective cohort study and were supplemented by data from the 9 A2ALL transplant centres.

Cohort study includes 821 patients – 385 of these received a transplant within the timeframe of the study period.

It is planned in a subsequent study to compare survival of those who received an LD transplant with those still on the waiting list.

68% of donors were blood relatives to their recipient

Outcomes are classified as early (first 90 days) or late (91–365 days).

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td>Number of patients analysed: 385 adults with LD liver transplantation

Recipient survival, graft survival, retransplantation

<table>
<tr><td></td><td>3 months</td><td>1 year</td></tr>
<tr><td>Survival</td><td>94%</td><td>89%</td></tr>
<tr><td>Graft survival</td><td>87%</td><td>81%</td></tr>
<tr><td>All deaths</td><td>22</td><td>20</td></tr>
<tr><td>Retransplants</td><td>32</td><td>5</td></tr>
<tr><td>Graft failures</td><td>51</td><td>21</td></tr>
</table>

The largest number of deaths was due to infection and sepsis (43%), followed by multiorgan failure, graft failure and cardiopulmonary causes.

21 patients died with a functioning graft.
7 patients died following retransplantation: in 27 (3.5%) of the LD group and 49 (3.3%) of the CAD group.</td><td>Complications:

<table>
<tr><td></td><td>Early</td><td>Late</td></tr>
<tr><td>Infection</td><td>123 (32%)</td><td>30 (8%)</td></tr>
<tr><td>• bacterial</td><td>107 (28%)</td><td>18 (5%)</td></tr>
<tr><td>• fungal</td><td>34 (9%)</td><td>1 (0.3%)</td></tr>
<tr><td>• viral</td><td>9 (2%)</td><td>6 (2%)</td></tr>
<tr><td>Ascites</td><td>48 (12%)</td><td>5 (1%)</td></tr>
<tr><td>Bile leak</td><td>117 (30%)</td><td>7 (2%)</td></tr>
<tr><td>Biliary stricture</td><td>29 (8%)</td><td>37 (10%)</td></tr>
<tr><td>Hepatic artery thrombosis</td><td>22 (6%)</td><td>2 (0.5%)</td></tr>
<tr><td>Hernia</td><td>6 (2%)</td><td>19 (5%)</td></tr>
<tr><td>Intra-abdominal abscess</td><td>27 (7%)</td><td>6 (2%)</td></tr>
<tr><td>Intra-abdominal bleed</td><td>26 (7%)</td><td>2 (0.5%)</td></tr>
<tr><td>Pleural effusion</td><td>70 (18%)</td><td>5 (1%)</td></tr>
<tr><td>Portal vein thrombosis</td><td>8 (2%)</td><td>3 (0.8%)</td></tr>
<tr><td>Pulmonary edema</td><td>38 (10%)</td><td>4 (1%)</td></tr>
<tr><td>Re-exploration</td><td>93 (24%)</td><td>2 (0.5%)</td></tr>
<tr><td>Upper/lower gastrointestinal bleed</td><td>26 (7%)</td><td>5 (1%)</td></tr>
</table>

Early complications occurred within first 3 months; late complications were those occurring 3 months–1 year.</td></tr>
<tr><td colspan="2">Abbreviations used: CAD, cadaveric; LD, living donor; NR, not reported; NS, not significant (as reported in the study); UNOS, United Network for Organ Sharing.</td></tr>
</table>

Study 8 Hwang S (2006)

Details

Study type	**Case series**
Country	Korea
Recruitment period	2000-2002
Study population and number	n= **259 LD liver transplant recipients**
Age and sex	Mean age 48 years (range 24–64 years). 79.5% males.
Selection criteria	Population: The most common primary diagnosis: hepatitis-B-associated liver cirrhosis Indications: Dual graft transplants, perioperative mortality and retransplant cases were excluded.
Technique	Right (n = 225) and left lobe liver (n = 34) grafts
Follow-up	**Mean 46 months (range 5–68 months)**
Conflict of interest/source of funding	None declared

Analysis

Study design issues: This study reported on adult-to-adult outcomes.

Study only reported on biliary complications following adult LD liver transplantation.

The majority of grafts were right liver grafts and this reflects current practice.

Authors introduced duct-to-duct anastomosis as part of their management of biliary complications.

Other issues: Authors noted that their management policy differed from that of other liver donor programmes – this may have an impact on the generalisability of the findings. However, the initial incidence of biliary complications should be similar to other centres.

Authors suggested that their higher rates of biliary complications compared with previously reported rates is due to the longer follow-up of this study.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: 259 **LD liver transplant recipients (efficacy not the aim of the paper)** **Recipient survival** As of August 2005, 236 (91.1%) of the 259 patients were alive. 1-, 3- and 5-year survival rates were 96.1%, 91.9% and 91.2%, respectively. **Donor outcomes: not reported.**	**Complications**: Deaths Main causes of death: • recurrence of HCC (7) • rejection (6) • infection (4). Morbidity There were 3 biliary complications in 2/34 left liver grafts, whereas there were 51 occurrences in 48/225 right liver grafts. Authors noted that incidence of biliary complications at 1 and 3 months was 4.7% and 8.9%, respectively. There were 11 anastomotic leak cases most occurring within the first month. 1-, 3- and 5-year biliary-complication-free survival for the right liver group was 85.1%, 79.4% and 77.3%, respectively, and for left liver group 97%, 97% and 93.6%, respectively (p=0.024). For the entire group, cumulative 1-, 3- and 5-year biliary complication rates were 12.9%, 18.2% and 20.2%, respectively.
Abbreviations used: CAD, cadaveric; LD, living donor; NR, not reported; NS, not significant (as reported in the study); UNOS, United Network for Organ Sharing.	

Table 4 Summary of key efficacy and safety findings on living-donor liver transplantation (donor safety)

Study 9 Cheah YL (2013)

Details

Study type	Survey
Country	Worldwide (21 countries: 39 centres in North America, 13 in Asia, 13 in Europe, 4 in South America, 1 in Middle East, and 1 in New Zealand))
Recruitment period	not reported
Study population and number	n=**148 Living Donor Liver Transplant (LDLT) programmes reporting donor outcomes** 71 programmes completed survey (currently only 64 centres perform LDLT; 54 both adult-to-adult and adult-to paediatric, 5 only adult and 5 only paediatric) **n=11553**
Age and sex	Not applicable
Selection criteria	All liver transplant programmes known to have performed LDLT at least once (from 1983-2007). Programme lists obtained from published literature, the American Society of Transplant Surgeons, the Japanese Liver Transplant Society, the European Liver Transplant Registry and the China Transplant Registry. Additional programmes were included if they were known by authors to be performing LDLT.
Technique	Living-donor hepatic lobectomy
Follow-up	**Not reported**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: follow-up emails, phone calls and personal interaction were used to increase survey completion. Only 48% (71/148) of the programmes completed the survey. Authors state that it is likely that inactive programmes did not respond.

Study design issues: survey aimed to obtain comprehensive data on the incidence of adverse events after LDLT. Email requests were used to recruit participants. Data is retrospective, self-reported and based on a web-based survey tool (Survey Monkey). The length of the survey was respondent driven. Participants were asked to provide programme demographics, donor evaluation information, donor morbidity and mortality data and the incidence of near-miss events and donor aborted hepatectomy. The validated Clavien system for grading of surgical complications was modified for living donors and they were provided with a survey to report the percentage of events that occurred and the rate of severity. For near miss and Clavien grade III-V, details of incidents were reported.

The survey was considered complete if >80% of items were completed (according to American Survey Research Organisation standards). Results were reported by the authors in a blinded manner.

Other issues: Authors suggest that this report may not represent a comprehensive assessment of living donor risks as it is retrospective and subject to variations by each centre's definition of adverse events.

Key efficacy and safety findings

Safety

Number of patients analysed: 71 programmes (n=11553)

Donor mortality reported in survey: 0.2% (23/11553), includes 6 deaths (2 from lung cancer, 1 from asthma, 1 from myocardial infarction at 6 years and 2 late suicides) unlikely to be related to donor surgery. There was no association between the type of donor hepatectomy (right versus left versus left lateral segment) and the incidence of death (p=NS for all groups).

Cause of death -total 23	**Location**	**Lobe**	**Timing**
Intraoperative			
Bleeding/cardiac failure/cardiac arrest	North America	Right	0 days
Early postoperative (<60 days)			
Anaphylaxis	North America	Left lateral segment	1 day
Pulmonary embolism	Europe	Left lateral segment	2days
Gastric necrosis (*Clostridium perfringens*)-fulminant and fatal gas gangrene of the stomach	North America	Right	3 days
Cardiac arrest	North America	Right	4 days
Myocardial infarction	Asia	Right	10 days
Sepsis/multi-organ failure	Europe	Right	11 days
Sepsis/multi-organ failure	Europe	Right	21days
Fall at home	Asia	Right	28 days
Cardiac failure/liver transplantation performed but failed	Europe	Right	32 days
Subarachnoid haemorrhage	Asia	Right	42 days
Multi-organ failure	Europe	Right	49 days
Complications of multiple myeloma	Europe	Right	56 days
Bile peritonitis/sepsis/multi-organ failure	Middle East	Right	60 days
Suicide	North America	Left	60 days
Late postoperative (>60 days)			
Duodenal-inferior vena cava fistula (ulcer)/air embolism	Asia	Right	2.3 months
Non-alcoholic steatohepatitis/liver failure/liver transplantation performed but failed	Asia	Right	9 months
Lung cancer	Asia	Right	22 months
Lung cancer	Asia	Right	3.4 years
Suicide	South America	Right	4 years
Suicide	South America	Left lateral segment	5 years
Asthma	Asia	Right	5 years
Myocardial infarction	Asia	Left	6 years
Deaths published but not captured in survey (but reported in this study by authors)			
Early postoperative (<60 days)			
Cardiac arrest/persistent vegetative state	Asia	Right	2 days
Cardiac arrhythmia	South America	Right	2 days
Massive bleeding	Europe	Right	4 days
Subarachnoid haemorrhage	South America	Right	7 days
Unknown	Asia	Unknown	10 days
Bile leak/sepsis/multi-organ failure	North America	Right	3 weeks
Berardinelli-Seip/liver transplantation/cardiac failure	Europe	Right	32 days
Pulmonary embolism	North America	Left	Unknown
Late postoperative (>60 days)			

Suicide	North America	Right	22 months
Suicide	North America	Right	23 months
Acute Budd-Chiari syndrome	Europe	Unknown	Unknown

Donor aborted hepatectomy (AH), defined as any procedure stopped after the donor entered the preoperative area

	Centres responded n (%)	**Cases n (%)**
Total	**44/71 (62)**	**136/11553 (1.2)**
Donor related		**106/136 (77.9)**
Recipient related		**30/136 (22.1)**
Donor reasons		
Vascular anatomy	14	22
Biliary anatomy	10	20
Vascular and biliary anatomy	2	2
Hepatic steatosis	10	14
Intraoperative pathology	11	20
Haemodynamic instability	7	10
Pre-anaesthesia event	3	4
Airway issue	3	3
Tumour	2	2
Intraoperative liver injury	2	2
Small graft or remnant volume	3	3
Other (anaphylaxis, 1; withdrawal, 1; urethral stricture needing a suprapubic tube, 1; right hepatic artery dissection, 1)	4	4
Recipient reasons		
Malignancy	9	10
Haemodynamic instability	7	10
Death	4	4
Aborted hepatectomy (no further details available)	1	3
Other (tuberculosis, 1; gangrene bowel, 1; disseminated intravascular coagulation, 1	3	3

Majority occurred after incision but before bile duct transection (72%, 98/136). After AH, 45% (61/136) eventually donated, 55% (75/136) did not donate. Procedure related complications were experienced by 13% of the patients after AH, with incisional hernias and wound infections occurring most frequently.

Donor morbidity

	% (n)
Overall morbidity*	**24 (2780/11553)**
Donors requiring liver transplantation (2 were secondary to hepatic failure related to hepatic vein thrombosis; 2 died despite transplantation)	0.009% (n=4)

*Most events occurred within the first 30 postoperative days. Most common complications were bile leaks, wound infections, incisional hernias and unplanned surgical re-exploration. Majority were mild and self-limited (Clavien grade I or II).

Near-miss events (defined as an event or events with potentially fatal consequences that are successfully managed with no lasting ill effects).

Near-miss events	**Centres n**	**Events n (%)**
Total		**126/11553 (1.1)**
Reoperation for bleeding	20	39
Biliary reconstruction	11	17

Portal vein thrombosis	10	10
Inferior vena cava/hepatic vein thrombosis	4	5
Pulmonary embolism	7	9
Reoperation for intra-abdominal sepsis	6	7
Transient liver insufficiency	5	6
Transient hemodynamic instability	1	1
Vascular reconstruction for injury	4	4
Reoperation for bowel injury	3	3
Myocardial infarction	3	3
Transplantation (liver, 2; kidney, 1)	3	3
Massive intraoperative bleeding (secondary to clamp failure)	5	5
Anaphylaxis/systemic inflammatory response syndrome	2	2
Respiratory failure requiring mechanical ventilation	3	3
Reoperation for diaphragmatic hernia	2	2
Parietal transient ischemic attack with motor weakness and foot drop	1	1
Gastric volvulus (after left lobe donation)	2	2
Cardiac arrest	1	1
Endocarditis	1	1
Reoperation for perforated gastric ulcer	1	1

Impact of programme experience (volume) on donor outcomes

	Incidence % (mean ± SD)			**P value**		
	Group 1 (<50LDLTs)	**Group 2 (51-200LDLTs)**	**Group 3 (>200 LDLTs)**	**group 1 vs group 2**	**group 1 vs group 3**	**group 2 vs group 3**
Near-miss events	2.9±15.7	1.8±6.5	0.5±0.3	0.11	<0.001	<0.001
Overall morbidity	23.2±15.4	24.1±12.2	25.0±15.3	0.81	0.74	0.85
Clavien grades III-V	8.1±11.8	8.3±9.4	10.7±12.1	0.95	0.54	0.51
AH	3.8±23.1	1.5±0.9	0.7±0.8	<0.001	<0.001	<0.001
Liver transplantation	0.15±0.2	0.03±0.03	0.02±0.1	0.59	0.73	0.61
Death	0	0.2±0.03	0.1±0.9	0.52	0.78	0.40

Abbreviations used: AH, aborted hepatectomy; LDLT, living donor liver transplantation; NS, not significant; SD, standard deviation.

Study 10 Muzaale AD (2012)

Study type	Matched case-control national study
Country	USA
Recruitment period	1994–2011 (over 17 years)
Study population and number	n=**4111 live liver donors (entire cohort in USA)** Relation to recipient: biological relative 77%, spouse 6%, non-biologically related individual 17%.
Age and sex	90% (3691/4111) younger than 50 years 49% (2017/4111) male.
Patient selection criteria	All adult healthy live liver donors as reported to the Organ Procurement and Transplantation Network (OPTN) were included. Patients who participated in domino liver transplantation were excluded (n=117) from the analysis.
Technique	Living donor liver transplantation (LDLT) - left lateral segment 24% (n=996), left lobe 9% (n=359), right lobe 67% (n=2742).
Follow-up	**Mean 7.6 years (range 4.2-10.1 years)**
Conflict of interest/source of funding	Authors disclose no conflicts. The Organ Procurement and Transplantation Network (OPTN) is supported by health resources and service administration contract 234-2005-370011C.

Analysis

Study design issues: study estimated the risk of early death and acute liver failure and long term mortality by comparing survival data with live kidney donors and healthy participants of the National Health and Nutrition Examination Survey (NHANES) III. Live kidney donors were chosen as a comparator because long-term survival data were available and they would represent as closely as possible the health of live liver donors.

Details of early death, acute liver failure and liver transplant for live donors since 1999 were taken from the OTPN for analysis; early and late deaths for study period were augmented by linkage to Social Security Death Master File (SSDMF). Early deaths identified by only SSDMF were confirmed with transplant centres.

Live kidney donors were matched with live liver donors using iterative radius matching techniques (i.e. age, sex, race, background, BMI, had rigorous screening).

The study compared the mortality risks associated with the portion of liver donated (left lateral segment or left lobe versus right lobe donation). Long-term mortality of live liver donors was compared with healthy matched controls.

Study population issues:

These deaths are mentioned in other publications (Cheah 2012 in table 2).

Key efficacy and safety findings

Safety

Number of patients analysed: **4111 live liver donors**

Early death and acute liver failure after LDLT

	Early death (within 90 days)			Early death or acute failure (catastrophic events)		
Cohort^	**n**	**Rate* (95% CI)**	**p value**	**n**	**Rate (95% CI)**	**p value**
Liver donor	7	1.7(0.7-3.5)		11 (7 early deaths, 4 acute liver failure [ALF] in right lobe donors): • 3 ALF 2–3 days after donation-needed rescue DDLT, • 1 sub-fulminant liver failure 7 days after donation-recovered).	2.9 (1.5-5.1)	
Kidney donor	2	0.5 (0.1-1.8)	0.09		N/A	
NHANES III controls	0	0.0 (0.0-0.9)	0.008		N/A	
Sub-group analysis						
Recipient age			0.9			0.4
Child	2	1.6 (0.2-5.8)		2	1.6 (0.2-5.8)	
Adult (>17 years old)	5	1.7 (0.6-4.1)		9	3.1 (1.4-6.0)	
Lobe/segment resected			0.8			0.9
Left lateral segment	2	2.0 (0.2-7.3)		2	2.0 (0.3-7.8)	
Left lobe	1	2.8 (0.1-15.5)		1	2.8 (0.1-15.5)	
Right lobe	4	1.5 (0.4-3.7)		8	3.3 (1.5-6.2)	
Donation year^^			0.8			1.0
1994–1998	1	2.9 (0.1-16.4)		1	2.9 (0.1-16.4)	
1999–2002	2	1.3 (0.2-4.8)		4	2.6 (0.7-6.7)	
2003–2010	4	1.8 (0.5-4.7)		6	2.7 (1.0-6.0)	

*rate per 1000 donors (derived using Poisson exact intervals 95% CI and x^2 tests, p values reported)

^matched cohorts identified from live kidney donors and eligible NHANESIII survey participants

^^1994–98, adult to child LDLT was the main procedure performed in USA (92%, 325/354), in 1999-2002, adult-to-adult LDLTs (mainly right lobe) were performed in 72% (1111/1523) and in 2003-10, adult to adult LDLTs were performed in 77% (1689/2187).

Cause of perioperative mortality after LDLT

Donor	Donated lobe	Days to death	Cause of death
1 (adult –to-child)	Left lateral	2	Anaphylaxis
2 (adult-to-adult)	Right lobe	21	Multi-organ failure
3 (adult-to-adult)	Right lobe	3	Infection
4 (adult-to-child)	Left lateral	58	Overdose
5 (adult-to-adult)	Left lobe	71	Suicide
6 (adult-to-adult)	Right lobe)	0	Cardiovascular
7 (adult-to-adult)	Right lobe	4	Respiratory arrest

Long term mortality (early and late deaths) (median follow-up 7.6 years and 29,965 person-years) (Kaplan-Meier curves)

Overall 31 deaths occurred at a rate of 1.4 deaths per 1000 person-years, 24 of these deaths occurred beyond 90 days.

Cumulative long term mortality of live liver donors (n=4111) was comparable to that of live kidney donors and NHANES control participants at 2 years (0.3%, 0.2%, and 0.3%) 5 years (0.4%, 0.4%, 0.4%) and 11 years (1.2%, 1.2% and 1.4%) respectively (p=0.9).

Abbreviations used: CI, confidence interval; DDLT, deceased donor liver transplantation LDLT, living donor liver transplantation; NHANES, National Health and Nutrition Examination Survey.

Study 11 Middleton PF (2006) (included in previous overview)

Study type	Systematic review
Country	Australia
Recruitment period	1990-2004
Study population and number	n=**214 studies (307 articles, 6000 procedures), specifically looking at donor outcomes** Authors noted that most of the studies were case series, with some comparative studies using contemporary or historical controls.
Age and sex	Not reported
Study selection criteria	All studies using any surgical technique for transplanting a liver from a live adult (> 18 years) donor to an adult or child recipient were included. Comparative studies, registry data, or case series were included without language restriction.
Technique	Articles reporting on adult to adult living donor liver transplantation (A-A LDLT)
Follow-up	**Unclear (maximum follow-up appears to be 6 months)**
Conflict of interest/source of funding	None declared

Analysis

Study design issues: The systematic review specifically looked at the donor outcomes.

The authors estimated that about 6000 living donor liver transplant procedures have been performed worldwide to the date of the study.

The authors estimated mortality rates. Rates were based on the published literature but the authors noted that these may be overestimates due to duplicate reporting or underestimated due to publication bias.

Donor yield was also reported in the review. However, this was not extracted here.

The systematic review reported that relatively few studies had assessed donor quality of life and psychological outcomes. Most of these studies used different measures, which made it difficult to collate and draw conclusions.

There were studies that also compared live donor liver transplantation with deceased donor liver transplantation.

Other issues: The authors noted that there appeared to be some suggestion that some right lobe donors may not be left with sufficient liver reserve.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **217 studies on LDLT** **Operation duration (donor)** 205–762 minutes, median 423 minutes (52 studies). **Return to work (donor)** Return to work or normal activity was close to 100% at 3–6 month follow-up (18 studies). **Liver function (donor)** Donor liver function normalised in a timeframe of weeks to months after LDLT (generally about a week after LDLT) (63 studies). **Liver regeneration in donor** The non-transplanted part of the donor liver regenerated to about double the size of their remnant liver within several months, reaching a median 89% of the original size (follow-up 7 days to 6 months) (16 studies). **Donor quality of life** Eight studies reported on quality of life. Authors noted that it was difficult to collate data because of the small number of studies and the variety of tools used to measure quality of life. **Psychosocial outcomes** The authors noted that summation of these findings was difficult. 6 studies reported on depression in donors following transplantation (rates between 0.2–15%). **Donor satisfaction and attitudes** All donors reported no coercion to donate. 8 studies reported that a median of 100% of LDLT donors would donate again (range 78–100%). 90–100% of donors believed that LDLT was a useful procedure (12 studies). 85% of donors stated that information made available was 'adequate'. 29–38% donors felt recovery was longer than expected (3 studies), 30–55% found the pain worse than expected (3 studies) and 30–40% donors reported that the surgical scar was worse than expected (2 studies).	**Complications**: **Mortality** Authors estimated that there were 12–13 donor deaths following live liver transplantation (0.2%) (117 studies): • At least 7 involving adult-to-adult donation (sepsis, 3; massive bleeding, 1; pulmonary embolism, 1; liver insufficiency, 1; multiple postoperative complications, 1). • At least 3 involving adult-to-child donations (pulmonary embolism, 1; anaesthetic complications, 1; multiple organ failure, 1). • 3 late donor deaths (one from acute Budd-Chiari syndrome caused by remnant liver torsion and other 2 reasons not reported). Authors noted that mortality for donation of a left lobe (0.05–0.21%) was potentially lower than for right lobe donation (0.23–0.5%). One was left lateral segment and there were 3 unspecified graft types. **Morbidity** Donor morbidity was reported in 131 studies and ranged from 0% to 100% with a median of 16.1%. Biliary complications (leaks and strictures) and infections were the most commonly reported morbidities. Rates of infections were reported in 50 studies and ranged between 0% and 28.6%. The median reported infection rate was 5.8%. The median biliary complication rate (biliary leakage and biliary stricture) was 6.2% (rates ranged from 0–39%; based on 97 studies). These were most commonly wound infections, urinary tract infections, pneumonia and other infections. **Blood loss and transfusion** Donor blood loss ranged from 72 ml to 2000 ml, with a median of 588 ml (55 studies). Blood transfusion was required in a median of 1.9% of donors, ranging from 0% to 80% across 57 studies.
Abbreviations used: LDLT, living donor liver transplantation.	

Study 12 Hashikura Y (2009)

Study type	Survey (Japanese Liver Transplantation Society Registry)
Country	Japan
Recruitment period	1988–2006
Study population and number	n= **4294 living donor liver transplantation (LDLT) donors (55 centres)** Population: LDLT donors and recipients in the Japanese Liver Transplantation Society Registry (all centres in Japan report characteristics and results of all donors and recipients, including deaths and severe complications).
Age and sex	Not reported
Patient selection criteria	Aborted donations were not included in the analysis.
Technique	Living donor hepatic lobectomy
Follow-up	**18 years**
Conflict of interest/source of funding	None declared

Analysis

Follow-up issues: Centres that did not respond were contacted up to 3 times by email or phone. 31% (17/55) centres did not respond to the survey. The authors state that the complexity of the questionnaire might have led to low response rates.

Study design issues: This is a retrospective medical record review of outcomes in living liver donors. All major LDLT centres were included in the study. Study was designed based on the registry database data.

Data collected on transplantations performed up to 2006 and followed up for at least 1 year (until 2007).

A detailed questionnaire was sent to all centres with liver transplantation programmes in Japan. Data on all donor hepatectomies, results for donors, including preoperative, postoperative complications, incidence of reoperation, severe adverse effects and death were collected. Data on any change in institutional policy related to preoperative evaluation, operative techniques, or postoperative management were also collected.

The validated Clavien system was used to standardise data collection from different programmes on complications. Data were collected only on Clavien grades II-V, and grade I events were not included as it was considered unfeasible in this large cohort.

Other issues: The authors state that severe complications and deaths were reported accurately to the database and have been investigated by the Society. They suggest that donor morbidity might have been underestimated due to the lack of a complete reporting system.

Key efficacy and safety findings

Safety

Number of patients analysed: **3565 LDLT donors from 85% (38/55) centres**

Type of graft	**number of donors (n)**
Lateral segment	1045
Left lobe	1088
Right lobe	1378
Right lateral sector	54
Total	**3565**

Complications:

	n (%)
Intraoperative problems	**27**
Homologous blood transfusion (for hepatic vein injury)	16
Biliary stricture	6
Malignant hyperthermia	1
Bronchial asthma	1
Thrombosis in the inferior vena cava	1
Cervical vein injury	1
Ventricular tachycardia	1
Postoperative complications	**270/3565 (8%)**
Bile leakage	94 (2.6)
Wound infection	44 (1.2)
Gastric outlet obstruction	27 (0.8)
Biliary stricture	13 (0.4)
Homologous blood transfusion	10 (0.3)
Small bowel obstruction	10
Brachial plexus palsy	9
Gastro-duodenal ulcer	9
Pleural effusion	9
Intra-abdominal abscess	6
Psychological problems	5
Alopecia	4
Incisional hernia	4
Atelectasis	3
Hoarseness	3
Liver dysfunction (needing admission to ICU)	3
Intestinal perforation	2
Portal vein thrombosis	2
Pneumothorax	2
Achalasia recurrence	1
Cardiac failure	1
Chylous ascites	1
Hepatitis C	1
Hypertrophic scar	1
Peroneal nerve palsy	1
Pneumonia	1
Severe wound pain	1

Clavien grade IVb	**2/3565 (0.06)**
Temporary multi-organ failure (patient had biliary stricture and infection that led to this event)	1
Paralysis of the lower body for more than 2 years (patient had BMI 34, and high risk of thrombotic complications, an overdose of heparin was administered, epidural hematoma confirmed on postoperative day 1).	1
Clavien grade V- Death (in a RL donor after 6 months due to NASH and an excessively small remnant liver volume; patient had domino liver transplantation at 5 months and died 1 month later).	**1/3565 (0.03)**
Total (overall morbidity)	**297 (8.3)**

Of the 270 postoperative complications, 125 were Clavien grade II, 86 were grade IIIa, and 56 were IIIb.

Incidence of postoperative donor complications according to graft type

Graft type	Incidence of donor complications %
Right lobe (n=1378)	9.4
Left lobe (n=1088)	8.7
Lateral segment (n=1045)	3.5
Right posterior segment (n=54)	14.8

The severity of postoperative complications between right and left lobe donors

Clavien grade	Right lobe (n=1088) %	Left lobe (n=1378) %
II	3.6	5.2
IIIa	3.6	2.0
IIIb	2.1	1.5
IVa	0	0
IVb	0.1	0.1
v	0.1	0

Incidence of reoperation

Reoperations were needed in 1.3% (48/3565) donors, including repeat biliary reconstruction, adhesiolysis and closure of bile duct leakage.

Changes in institutional policy

10.4% (311/299) events led to changes in policy for donor operations. These involved changes or attempts to improve preoperative evaluation, hepatic resection technique and postoperative care.

Abbreviations used: BMI, body mass index; ICU, intensive care unit; LDLT, living donor liver transplantation; NASH, non-alcoholic steatohepatitis; RL, right lobe.

Study 13 Lo CM (2003) (included in previous overview)

Study type	Case series (based on survey results)
Country	Hong Kong, China, Korea, Japan (5 Asian centres)
Recruitment period	1990–2001
Study population and number	n=**1508 living-donor liver transplant donors** **recipients included 766 adults and 742 children (< 18 years)** The most common relationship was parents (53.2%).
Age and sex	90.4% of donors were younger than 50 years. Male to female ratio was 1:1.2.
Patient selection criteria	Indications: Upper age limit of 65 years. 3 centres did not accept friends or unrelated persons as donors.
Technique	Living donor liver transplantation (LDLT) Right lobectomy or right lateral segment (561), left lateral or extended left lateral segment (605) or left lobe segmentectomy (334)
Follow-up	**Follow-up was greater than 3 months in 228 donors (15.1%)**
Conflict of interest/source of funding	None declared

Analysis

Study design issues: A questionnaire was sent to 5 participating liver centres to request information on annual statistics. However, the response rate is not reported.

All 5 centres participating in the survey performed more than 100 living donor liver transplantations.

The authors noted that in recent years there has been in an increase in the number of living donor liver transplants as a result of the increase in the use of right lobe grafts.

In terms of transplant technique 8 cases could not be classified.

Results were analysed in terms of technique: donors undergoing left lateral/extended left grafts; those undergoing left lobectomy; those undergoing right lobectomy or right lateral grafts. However, no statistical comparisons were undertaken to see if any significant differences existed in outcomes between the groups.

Other issues: The authors noted that it may not be appropriate to compare the results of the present survey on the Asian experience with those reported from Europe because of the differences in the donors such as body build, operative techniques and selection criteria.

Key efficacy and safety findings

Safety

Number of patients analysed: **1508 LDLT donors**

Mortality

There was no hospital mortality but there was 1 late sudden death during exercise in a donor 3 years after operation.

Complications:

There were 238 complications with an overall complication rate of 15.8%.

There were:

- 56 (9.3%) complications in donors undergoing left lateral or extended left lateral segment grafts.
- 25 (7.5%) complications in donors undergoing left lobe grafts.
- 157 (28%) complications in donors undergoing right or right lateral grafts. These included hyperbilirubinaemia and intra-abdominal fluid collection.

Authors noted that the right donor group also had more serious complications than the other 2 groups.

	n (%)
Biliary leakage and cholestasis (bilirubin>5 mg/dL)	75 (5)
Hyperbilirubinaemia	43 (2.9)
Intra-abdominal fluid collection	20 (1.3)
Small bowel obstruction	10 (0.6)
Biliary stricture	7 (0.5)
Portal vein thrombosis	3 (0.2)
Pulmonary embolism	4 (0.2)
Intra-abdominal bleeding	3 (0.2)
Pancreatitis	3
Bleeding duodenal ulcer	3
Incisional hernia	1
Renal failure (due to radiographic contrast medium	1
Gastric perforation	1
Wound infection	45 (3)
Gastric outlet obstruction	8
Pleural effusion	6
Pneumonia	3
Pressure sore	1
Peroneal nerve palsy	1
Total complications	**238 (15.8)**

Reoperations

1.1% (17/1508) donors underwent reoperation because of small bowel obstruction (n=3), bile duct stricture (n=3), bile leakage (n=3), intra-abdominal bleeding (n=3), portal vein thrombosis (n=2), ileus (n=2) and incisional hernia (n=1).

Abbreviations used: LDLT, living donor liver transplantation.

Study 14 Iida T (2010)

Study type	Retrospective case series (based on survey results)
Country	Japan (single high volume transplant centre)
Recruitment period	1990 -2007
Study population and number	n=**1262 living donor liver transplantation (LDLT) donors** Right lobe(RL) group (n=500; 426 RL-Middle Hepatic Vein (MHV), 74 RL+MHV), Left lobe group (n=762; 493 lateral segments, 180left lobe, 45 extended lateral segments, 44 monosegment grafts).
Age and sex	Median 36 years (range 18–66 years) 51% (639/1262) male
Patient selection criteria	Donor selection: voluntary, relationship with the recipient within the third degree of consanguinity or a spouse, no known medical disorder that may increase the perioperative risk and no history of malignant diseases. Donor age limit modified from 60 to 65 years after 2005 to expand donor pool. Evaluation by specialist in cardiology, chest disease and anaesthesia in donors aged 60 and older performed. Haemostatic model assessment index for donors with non-alcoholic steatohepatitis done. Posterior segment grafts donors and liver grafts from domino donors were excluded. For a RL graft without MHV a residual liver volume (RLV) of less than 30% and for RL with MHV an RLV of less than 35% of whole liver volume were excluded.
Technique	LDLT. All donors underwent routine postoperative heparinisation to prevent pulmonary embolism. Donor operation with right hepatectomy was modified in 2002 by placing a biliary decompression tube to prevent leakage from the bile duct stump and biliary stricture. Subsequently, in 2006, the method of bulk dissection of the Glisson pedicle at the hepatic hilus during the parenchymal transection was introduced to preserve blood supply to the bile duct both on the graft and donor side and prevent biliary stricture.
Follow-up	**Median 36.5 months (range 4–118 months)**
Conflict of interest/source of funding	None declared

Analysis

Study design issues: The demographic, operative and clinical data were collected during the postoperative period (4 weeks after surgery). The incidence of donor complications was assessed based on different time periods. The validated Clavien system was used to grade the severity of complications.

Other issues: Health related quality of life (HRQOL) outcomes for donors from the same centre are reported in the study below (Takada 2012).

Key efficacy and safety findings

Safety

Number of patients analysed: **1262 LDLT donors**

Overall complication rate: 26% (325/1262)

Short term complications (within 4 weeks) occurred in 24.4% (308/1262) donors

Medium term complications (4 weeks to 3 months) in 0.8% (10/1262) donors

Long term complications (after 3 months) in 0.6% (7/1262) donors.

Post-operative complications:

	Right lobe (RL) group % (n=500)	**Left lobe (LL) group % (n=762)**	**p value**
Total complication rate	44.2 (188/500) 221 events	18.8 (137/762) 143 events	<0.05
Total biliary complications	**12.2**	**4.9**	**<0.05**
Biliary leakage (1 RL donor needed prolonged placement of drainage tube)	10.6 (53)	4.7(36)	<0.05
Biliary stricture	1.6(8)	0.3(2)	<0.05
Other abdominal complications			
Fluid collection	9.2 (46)	0.9 (7)	<0.05
Skin wound infection	5.2 (26)	4.7 (36)	NS
Small bowel obstruction	2.6 (13)	1.9 (15)	NS
Intra-abdominal abscess	1.6 (8)	0.3 (2)	<0.05
Drug induced hepatotoxicity	1.2 (6)	0.8 (6)	NS
Massive ascites	1.0 (5)	0.1 (1)	<0.05
Hyperamylasaemia (>300 IU/L)	0.8 (4)	0.1 (1)	<0.05
Hyperbilirubinaemia	0.6 (3)	-	-
Gastric intractable ulcer	0.4 (2)	1.1 (8)	NS
Portal venous thrombosis	0.2 (1)	-	-
Liver failure (domino liver transplant performed but patient died)	0.2 (1)	-	-
Others	0.4 (2)	0.5 (4)	NS
Extra-abdominal complications			
Pleural effusion	4. 4 (22)	-	-
Pulmonary embolism (including suspected cases, I LL donor needed cardiopulmonary support and ICU management)	1.2 (6)	6.5 (5)	NS
Fever of unknown origin	0.6 (3)	1.1 (8)	NS
Others (1 RL donor needed blood transfusion for anaemia)	2.4 (12)	1.6 (12)	NS

Perioperative mortality: 0.08% (in 1 patient who had a domino transplantation for hepatic failure [caused by extended RL donation combined with underlying non-alcoholic steatohepatitis])

Complication severity according to graft type

Clavien grade	**RL group (n=500)**	**LL group (n=762)**
Grade I	46.4 (98)	12.7 (97)
Grade II	17.2 (38)	3.4 (26)
Grade IIIa	34.8 (77)	(15)
Grade IIIb	3.3 (7)	(4)
Grade IV	0	(1)
Grade V	0.5 (1)	0

The incidence of major complications (grade III-V) in RL and LL groups were 17% (85/500) and 2.6% (20/762).

Risk factors for postoperative complications

Multivariate analysis show that donor age (>40 years), right lobe donation and prolonged operation time (>400 min) were independent risk factors for complications.

Abbreviations used: ICU, intensive care unit; LDLT, living donor liver transplantation; LL, left lobe; NS, not significant; RL, right lobe;

Study 15 Takada Y (2012)

Study type	Case series (historical cohort study –based on survey results)
Country	Japan (single centre)
Recruitment period	1990–2004
Study population and number	n=**997 living-donor liver transplant (LDLT) donors**
Age and sex	Mean age 51 years
Patient selection criteria	Reported in study above (Iida 2010)
Technique	Living donor liver transplantation (LDLT)
Follow-up	**Mean post-donation period 6.8 years.**
Conflict of interest/source of funding	None declared

Analysis

Follow-up issues: 42% (419/997) of donors did not respond: 3 had bad health, 7 felt unmotivated, 4 had other reasons and reasons were unknown for 405 donors.

Study design issues: SF-36 survey was mailed to collect data from donors. The version 2 questionnaire, which included health related quality of life (HRQOL) scale and socio-demographic information, was used. Information about current comorbidities was collected and classified as having none, 1 or 2 or more.

Medical data were obtained from hospital database of LDLT donors. To allow easy comparison a norm-based scoring method was used to report the SF-36 results. The 8 subscale scores and 3 summary scores were transformed to norm-based scores with a mean of 50 and SD of 10 in the general Japanese population. HRQOL scores were stratified by year of donation and compared with those of Japanese norm populations.

HRQOL values were estimated after donation only, therefore changes in quality of life could not be estimated. The SF-36 questionnaire comprises 36 questions scored with 8 subscales. The 8 scales are summarised by 3 component summary scores: physical component score (PCS), mental component score (MCS) and the role/social component score (RCS).

The severity of complications was graded with the Clavien classification system. Japanese population data were obtained from SF-36 Japanese norm data studied in 2002.

Other issues: responders may not be representative of all donors.

Key efficacy and safety findings

Efficacy

Number of patients analysed:

Response rate: 58% (578/997)

367 Left side (LS) donors and 211 Right side (RS) donors

Long term donor HRQOL

Donors had better HRQOL scores after LDLT than the Japanese norm scores (scores>50) across all time periods (1990-2004). The physical domain scores (PCS) were better than other scores. The MCS and RCS values for the donors were comparable to and sometimes lower than the population norms.

Donor HRQOL scores stratified by severity of postoperative complications (mean)

	PCS	MCS	RCS
No complications	54.8	51.2	49.8
grade I	54.8	52.6	50.2
grade II	57.1	47.7	48.4
Grade ≥3	54.3	52.3	51.0

Comparison of HRQOL in LG and RG donors (mean ± SD)

	Total	LS donors (n=367)	RS donors (n=211)	p value
PCS	54.9±7.3	55.0±7.4	54.6±6.9	0.50
MCS	51.5±9.9	51.1±10.3	52.1±9.1	0.22
RCS	49.9±9.4	50.0±9.7	49.9±8.8	0.97

In comparison with left side donors, right side donors were significantly older, included a higher proportion of donors who were not parents, had longer hospital stays, higher rates and more severe grades of postoperative complications (all <0.001), higher incidence of rehospitalisation (0.002) and a higher recipient mortality rate (0.006).

Effect of comorbidities of HRQOL

The frequency of comorbidities was similar in the 2 groups. In comparison with the Japanese population with 2 or more comorbidities, the donors demonstrated, after LDLT, significantly better HRQOL scores for 6 of the 8 subscales and comparable scores for the other 2 subscales.

Factors predicting donor HRQOL after LDLT

Multivariate analyses revealed that age, the number of months to recovery to preoperative health status, hospital visits due to donation-related symptoms, rest from work related to donation in the past month and the existence of 2 or more current comorbidities was significantly associated with decreased HRQOL scores. Postoperative mortality and recipient death were not predictors of poor HRQOL.

Abbreviations used: HRQOL, heath related quality of life; LDLT, living donor liver transplantation; MCS, mental component score; PCS, physical component score; RCS, role/social component score; SD, standard deviation

Study 16 Zhang S (2012)

Study type	Systematic review and meta-analysis
Country	China
Recruitment period	not applicable
Study population and number	n=**11 studies [764 patients]** (all observational without randomisation or control groups, published between 2003-2011, 1 non-English study Chinese) **Right lobe living donor liver transplantation (LDLT) donors with or without middle hepatic vein (MHV)**
Age and sex	Mean age 51 years
Study selection criteria	Studies considered for inclusion were those that compared outcomes of procedures with and without the MHV. Multicenter and single-centre studies were used whether or not blinded and without language restrictions. Reviews, case reports or commentaries were excluded.
Technique	Right lobe LDLT with or without middle hepatic vein (MHV)
Follow-up	**Not reported**
Conflict of interest/source of funding	Supported by a grant from the Shanghai science and technology committee.

Analysis

Study design issues: Systematic review performed according to a pre-specified protocol guided by the meta-analysis of observational studies in epidemiology consensus statement and the preferred reporting items for systematic reviews (PRISMA) statement.

Search performed until April 2011 and proper strategies (electronic and manual) were used. Critical appraisal and data extraction done by 2 reviewers independently and disagreements were resolved by consensus. A third reviewer checked the accuracy.

Meta-analysis was consistent with recommendations from the Cochrane collaboration and PRISMA statement. Data were analysed using random effects and fixed effects models, and results presented as weighted mean differences (WMD) or relative risk (RR).

Review was based on small observational studies from medical centres worldwide, the number of studies and patients included in each subgroup analysis were small.

Postoperative donor liver function recovery was assessed according to 3 postoperative recovery indicators: peak values of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and total bilirubin (TB).

Biliary complications (biliary leakage and/or stricture), other abdominal complications (fluid collection, hyperbilirubinaemia, incisional hernia, wound infection, postoperative haemorrhage and liver failure) and extra-abdominal complications (pulmonary embolism, pleural effusion, pneumonia, and other vital organ complications) after liver transplantation were included in the analysis.

Other issues: Recipient outcomes on liver functional recovery are not presented in this overview.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **11 studies (746 patients)**

Meta-analysis results of donor liver functional recovery and hospital stay between right lobe LDLT 'with MHV' versus 'without MHV' groups

Outcome measure	Effect	Effect size	95% CI	p value	I^2 (%)
Liver functional recovery in donors	WMD	-2.88	-6.11,0.36	0.08	0
Subgroup analysis					
Peak value of ALT (5 studies)	WMD	9.75	-26.86, 46.37	0.60	0
Peak value of AST (6 studies)	WMD	5.80	21.20, 32.79	0.67	0
Peak value of TB (7 studies)	WMD	–3.10	-6.37, 0.17	0.06	0
Donor hospital stay (7 studies)	WMD	0.00	-0.61, 0.61	1.0	0

Safety

Meta-analysis results of donor complications between right lobe LDLT 'with MHV' versus 'without MHV' groups

Outcome measure	Effect	Effect size	95% CI	p value	I^2 (%)
Donor complications	RR	1.02	0.7, 1.45	0.90	0
Subgroup analysis					
Biliary complications (8 studies)	RR	0.74	0.40, 1.35	0.32	0
Other abdominal complications (6 studies)	RR	1.12	0.60, 2.10	0.72	0
Extra-abdominal complications (6 studies)	RR	1.36	0.75, 2.47	0.31	0

Abbreviations used: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; LDLT, living donor liver transplantation; MHV, middle hepatic vein; RL, right lobe; RR, risk ratio; TB, total bilirubin; WMD, weighted mean difference

Study 17 Sotiropoulos GC (2011)

Study type	Case series (based on survey results)
Country	Germany (single centre)
Recruitment period	1998-2007
Study population and number	n=**83 donors**
Age and sex	Median age 36 years, 52% (43/40) male
Study selection criteria	Only donors with at least 3 years follow-up, good command of German language, and permanent residents were included.
Technique	Right hepatectomy for adult LDLT –included right hepatectomy (segments 5-8) and cholecystectomy. No inflow occlusion was applied. Initially the middle hepatic vein (MHV) was preserved with the donor but subsequently, in donors with adequate remnant liver mass, the MHV was either procured with the graft or its major tributaries identified and reconstructed according to 3D-analysis. Donors were routinely examined up to 1 year postdonation and only when needed thereafter.
Follow-up	**Median 69 months (range 46–128 months)**
Conflict of interest/source of funding	None

Analysis

Study design issues: Donors were contacted by telephone and invited to complete a questionnaire regarding health status, satisfaction (assessed on a scale 1–10/worst–best), self-esteem (assessed as better-similar-worst after donation), willingness to donate (yes/no) and suggestions for improvement. In addition donor files and cholecystectomy specimens were reviewed.

Donor complications were reported according to both Dindo-Clavien and live donor Modified Essen classification systems. Psychological outcomes and long term impairments were captured in the Essen classification modified for liver donors.

Kaplan-Meier and logistic regression analyses were performed.

Other issues: Recipient outcomes are not reported in this overview.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **83 donors**

Response rate: 100%

Psychometric measurements

Satisfaction (assessed on a scale 1-10/worst-best)

Median satisfaction score was 8.

Self-esteem

	% (n)
Better	14 (12/83)
Similar	81 (67/83)
Worst*	5 (4/83)

*Recipients of all donors who reported worst self-esteem died.

Willingness to donate again:

	% (n)
Yes	94 (78/83)
No (with persistent problems)	6 (5/83)

Donors suggestions

47% (39/83) recommended improvements mainly on detailed informed donor consent and a centralised living donor liver registry.

Safety

Donor complications

Complication	**Dindo-Clavien classification**	**n**
Early complications		**13**
Wound infections	Grade 1	3
Psychological problems, treated with antidepressants and psychotherapy	Grade 3	3
Pleural effusion	IIIa	1
1 inferior vena cava thrombosis needing thrombectomy, intra-abdominal abscess needing drainage (1), and small bowel obstruction (1), recurrent pleural effusion (1), hernia repair (1) and paracentesis needing laparotomy (1)	IIIb	6
Other	**Essen classification**	
Gastro-oesophageal reflux needing medical treatment	va	2
Incisional discomfort	va	4
Severe depression needing antidepressants and regular follow-up	vb	3
Long term (median 69 months follow-up)		
Multiple liver lacerations and permanent deterioration of liver function (due to motor accident at 71 months; acceptable function so no intervention needed)		1
Lactose intolerance (not attributed to LDLT)		3

Current symptoms

	% (n)
Total	**53 (44/83)**
Intolerance to fatty meals and diarrhoea /persistent nausea or vomiting (needed changes to diet) (symptoms attributed to cholecystectomy done during LDLT)	31 (26/83)
Gastro-oesophageal reflux associated with left liver hypertrophy (due to weight loss of 9–12kgs after 10 years in 3 donors; 3 had PPIs, 1 changed eating habits).	9 (7/83)
Incisional discomfort requiring pain medications (4 had restriction in fitness; 2 had keloid scars)	6 (5/83)
Severe depression (needing antidepressant therapy and hospitalisation)	4 (3/83)
Rib pain affecting lifestyle (at 55 and 119 months)	2 (2/83)
Exacerbation of psoriasis (due to stress associated with surgery)	1 (1/83)

Regression analyses comparing donors with and without current complaints showed no statistical differences with respect to donor age, gender, early complications and follow-up time, young to old donation, recipients' diagnosis of malignancy and death of the recipient.

Donor intolerance to fatty meals and diarrhoea were associated with normal cholecystectomy specimens (p=0.001).

Abbreviations used: LDLT, living donor liver transplantation.

Study 18 Nadalin S (2006)

Study type	Case series (prospective analysis of 4 donor procedures halted due to death of the recipient intra-operatively)
Country	Germany
Recruitment period	1998-2005
Study population and number	n=**4 donors, 4 intended right living donor liver transplant (LDLT) recipients** (affected by neuroendocrine tumor metastasized to the liver (n=2), hepatitis C cirrhosis with hepatocellular carcinoma (n=1), cryptogenic cirrhosis (n=1) and suitable for LDLT as per pretransplant evaluation.
Age and sex	median age 55 years, 100% male
Patient selection criteria	Recipients suitable for LDLT as per pretransplant evaluation. Donors: who underwent standard preoperative evaluation for LDLT
Technique	Adult-adult LDLT
Follow-up	**range 16–53 months**
Conflict of interest/source of funding	Not reported

Analysis

Study design issues: intraoperative and postoperative data were collected prospectively.

Other issues: Author states that there are no set rules on how to manage these situations and presented a unique rare experience.

Key efficacy and safety findings

Safety

Number of patients analysed: 4 recipients and 4 donors

Recipient outcomes: All 4 recipients died intra-operatively and donor operation aborted.

At the time of recipient death, the donors' hepatic ducts divided and liver parenchyma fully or almost completely resected in all 4. In all cases vascular pedicles were still intact. The donor hepatectomy was aborted and in each case reconstruction of the donor biliary tract was performed to maintain the status of '**hepar divisum' (divided liver)**.

Donor outcomes after 'hepar divisum'

Donor	Number of transected ducts	Reconstruction method	Early complications	Late complications	Follow-up (months)
1	3	hepatic jujenostomy	Bile leak from resected surface and anastomosis (resection stitched and redo of HJ	cholangitis and stenosis of bile duct anastomosis at 44 and 51 months (percutaneous dilatation of hepatic jujenostomy)	53
2	1	duct to duct anastomosis	stenosis on day 6 (ERCP and stenting)	No	47
3	1	duct to duct anastomosis	No		19
4	3	hepatic jujenostomy	bile leak from resection (percutaneous drain)	No	16

All 4 donors had full recovery and returned to their presurgery quality of life at a follow-up of 14-53 months.

Abbreviations used: LDLT, living donor liver transplantation.

Efficacy

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.

Recipient survival/graft survival (children)

In a review of primary studies assessing outcomes following adult-to-child transplantation, six month actuarial survival was similar in the living donor and the cadaveric transplantation groups[1]. However, median 5-year survival was slightly higher in the living-donor group (92%) than in the cadaveric group (81%; based on 8 studies). This was also true for graft rates (median 5-year rate was 81% in the living-donor group compared with 73% in the cadaveric graft group).

Recipient survival/graft survival (adults)

The evidence for efficacy in adult-to-adult transplantation is based on a systematic review and a large case–control study[5,6]. No significant differences in 12 months recipient survival were found in 3 comparative studies included in the review (80-100% in the living-donor group and 75–90% in the cadaveric-graft group). In 65 studies with no comparator arms, median survival for living donor transplantation recipients was reported to be 85.2% (ranging from 43–100%) at variable follow-up of 1–36 months.

Graft survival was also reported in 3 comparative studies. At a follow-up of at least 12 months, graft survival was 75–89% in the living-donor groups compared with 73–89% in the cadaveric–graft groups. The rate of retransplantation was given in 38 non-comparative studies, with a median rate of 9.3% (range 0–26.7%; follow-up was not reported).

Similar recipient survival rates were reported in a case–control study of 2234 patients, 754 of whom had undergone living-donor transplantation. Two-year recipient survival was 79% in the living-donor group and 80% in the cadaveric-graft group. Two-year graft survival however was significantly lower in the living-donor group. Retransplantation rates were not reported in this study[6].

In another case series of 385 patients, 1-year graft survival was 81%. There were 72 graft failures in the first 12 months, 71% occurring in the first 3 months. Thirty-seven patients (9.6%) underwent retransplantation[7].

Donor outcomes (evidence reviewed in 2015)

Return to normal function

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)[12].

Liver functional recovery

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), 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)[16].

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)[11].

Liver dysfunction

A survey of living donors (n=3565) in 38 Japanese LDLT centres reported liver dysfunction in 3 donors needing admission to an intensive care unit[12].

A case series (survey) of 1508 LDLT donors reported hyperbilirubinaemia in 3% (43/1508) of right lobe liver donors[13].

Quality of life

A case series of 997 donors assessed the long-term health-related quality of life (HRQOL) of donors using the SF-36 health survey. Of 578 respondents (58%), HRQOL scores for donors were better than the Japanese norm scores (scores>50) across all time periods (1990–2004). The scores were similar for left lobe (n=367) and right lobe donors (n=211)[15].

Safety

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

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).[1] Higher rates of biliary complications were reported in 3 other studies ranging from 14% (7/51) to 34% (14/41)[2-4]. Other complications reported included portal vein and hepatic artery thrombosis.

In a systematic review of adult recipient outcomes, the median reported biliary complication rate was 22.2% (based on 75 studies)[5]. 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[8].

Donor outcomes (evidence reviewed in 2015)

Donor mortality

Donor mortality was 0.2% (23/11,553) in a worldwide survey of LDLT programmes (71 centres, 11,553 patients). Most deaths (15/23) occurred within 60 days, and all except 4 deaths (2 from lung cancer at 22 months and 3.4 years, 1 from asthma at 5 years, 1 from myocardial infarction at 6 years) were related to the surgery. With these deaths excluded, the mortality rate was 0.16%[9].

Overall donor mortality was 0.2% (13/6000 procedures, 117 studies) in a systematic review of donor outcomes (n=214 studies) [11]. At least 7 deaths involving adult-to-adult donation (sepsis, 3; massive bleeding, 1; pulmonary embolism, 1; liver insufficiency, 1; multiple postoperative complications, 1); 3 involving adult-to-child donations (pulmonary embolism, 1: anaesthetic complications, 1; multiple organ failure, 1) and 3 late deaths (1 from acute Budd-Chiari syndrome caused by remnant liver torsion and reasons for the other 2 cases not specified) were reported. Mortality for donation of a left lobe (0.05–0.21%) was lower than for right lobe donation (0.23–0.5%)[11].

The risk of early death among donors was estimated as 1.7 per 1000 donors (95% CI 0.7 to 3.5) in a matched case-control study of 4111 donors over a mean follow-up of 7.6 years. There were 7 early donor deaths and the risk of death did not vary with age of the recipient (p=0.9), or portion of liver donated (p=0.8). There were 11 catastrophic events (7 deaths and 4 acute liver failures) and the risk of these events was 2.9 per 1000 donors (95% CI 1.5 to 5.1). Risk did not vary with age of the recipient (p=0.4), or portion of liver donated (p=0.9). Long-term mortality of live liver donors was comparable to that of live kidney donors and NHANES participants (controls; 1.2%, 1.2% and 1.4% at 11 years respectively, p=0.9)[10].

Overall donor morbidity

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. 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. Short-term complications (within 4 weeks after surgery) occurred in 24% (308/1262) of donors and medium- (4 weeks to

3 months) and long-term complications (after 3 months) were rare and occurred only in 1.5% (17/1262) of donors[14].

An overall morbidity rate of 15.8% (238/1508) was reported in a large case series (multicentre survey) of 1508 patients. The frequency of postoperative complications was significantly higher in donors of right lobe grafts (28%) compared with donors of left lobe grafts (7.5%)[13].

A systematic review of 11 studies comparing right lobe LDLT with or without the middle hepatic vein (MHV) reported that removal of the MHV did not affect morbidity rate in right lobe donors (p=0.90; RR=1.02)[16].

Severe life-threatening complications

Severe life-threatening complications were reported in 0.06% (2/3565) of donors (1 had multi-organ failure, 1 had lower body paralysis) in the survey of living donors in 38 Japanese LDLT centres[12].

Near-miss events (defined as an event or events with potentially fatal consequences that are successfully managed with no lasting ill-effects)

The overall incidence of near-miss events in donors was 1% (126/11,553) in the worldwide survey of LDLT programmes (71 centres). 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)[9].

Transplantation

Transplantation was needed in 0.04% of donors (5/11,553) after liver donation in the worldwide survey of LDLT programmes (71 centres). 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[9].

Biliary complications

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)[14].

Biliary complications were the most commonly reported donor morbidity, with a median rate of 6.2% (rates ranged from 0–39%; based on 97 studies), in the systematic review of donor outcomes (214 studies)[11].

Bile leakage and biliary strictures occurred in 5% (75/1508) and 1.1% (7/1508) of right lobe liver donors in the case series (multicentre survey) of 1508 LDLT donors[13].

Biliary leakage and biliary strictures were reported postoperatively in 2.6% (94/3565) and 0.4% (13/3565) of donors in a survey of living donors in 38 Japanese LDLT centres[12].

Infections

Infections occurred at a median rate of 6% (range 0–29%, based on 50 studies), in the systematic review of donor outcomes (214 studies)[11]. These were most commonly wound infections, urinary tract infections and pneumonia[11].

Wound infections were reported in 3% (45/1508) of right lobe liver donors in a case series (multicentre survey) of 1508 LDLT donors[13] and in 1.2% (44/3565) of donors in the survey of living donors in 38 Japanese LDLT centres[12].

Hepatitis C was reported in 1 patient in the survey of living donors (n=3565) in 38 Japanese LDLT centres[12].

Intra-abdominal abscess was reported in 0.8% (10/1262) of donors in the retrospective case series of 1262 patients at a median follow-up of 36.5 months[14]. The incidence was significantly higher in the right lobe group than in the left lobe group (1.6% versus 0.3%, $p<0.05$)[14].

Intra-abdominal sepsis requiring reoperation was reported in 7 donors in the worldwide survey of LDLT programmes (n=71 centres)[9].

Bowel obstruction

Gastric outlet obstruction was reported in 0.8% (27/3565) of donors in the survey of living donors in 38 Japanese LDLT centres[12] and in 0.5% (8/1508) of right lobe liver donors in a case series (multicentre survey) of 1508 LDLT donors[13].

Small bowel obstruction was reported in 2% (28/1262) of donors in the retrospective case series of 1262 patients at a median follow-up of 36.5 months[14] and in 0.6% (10/1508) of right lobe liver donors in the case series (multicentre survey) of 1508 LDLT donors[13].

Ascites or intra-abdominal fluid collection

Intra-abdominal fluid collection was reported in 4% (53/1262) of donors in the retrospective case series of 1262 patients at a median follow-up of 36.5 months[14]. The incidence was significantly higher in right lobe donors than in left lobe donors (9.2% versus 0.9%, $p<0.05$)[14].

Massive ascites was reported in 0.5% (6/1262) of donors in the retrospective case series of 1262 patients at a median follow-up of 36.5 months[6]. The incidence of ascites was significantly higher in the right lobe group than in the left lobe group (1.0% versus 0.1%, p<0.05)[14].

Chylous ascites was reported in 1 patient in the survey of living donors (n=3565) in 38 Japanese LDLT centres[12].

Haemorrhage

Massive intraoperative bleeding (secondary to clamp failure) was reported in 39 donors in the worldwide survey of LDLT programmes (n=71 centres)[9]. Haemorrhage needing surgical intervention was reported in 5 of 11,553 donors in the same study[9].

Intra-abdominal bleeding

Intra-abdominal bleeding occurred in 0.2% (3/1508) of right lobe liver donors in the case series (multicentre survey) of 1508 LDLT donors[13].

Bleeding duodenal ulcer was reported in 0.2% (3/1508) of right lobe liver donors in the case series (multicentre survey) of 1508 LDLT donors[13].

Pancreatitis

Pancreatitis occurred in 0.2% (3/1508) of right lobe liver donors in the multicentre survey of 1508 LDLT donors[13].

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[14]. The incidence of hyperamylasaemia was significantly higher in right lobe donors than in left lobe donors (p<0.05)[14].

Gastric complications

Gastric perforation occurred in 1 right lobe liver donor in the multicentre survey of 1508 LDLT donors[13].

Gastric volvulus was reported in 2 donors in the worldwide survey of LDLT programmes (n=71 centres)[9].

Perforated gastric ulcer was reported in 1 donor in the worldwide survey of LDLT programmes (n=71 centres)[9].

Thrombotic events

Thrombotic events (including portal vein, inferior vena cava or hepatic vein thrombosis and pulmonary embolism) were reported in 0.2% (24/11553) of donors in the worldwide survey of LDLT programmes (n=71 centres)[9].

Pulmonary embolism was reported in 0.9% (11/1262) of donors in the retrospective case series of 1262 patients at a median follow-up of 36.5 months[14].

Renal failure

Renal failure due to radiographic contrast medium was reported in 1 right lobe liver donor in the multicentre survey of 1508 LDLT donors[14].

Cardiac complications

Cardiac arrest and endocarditis were reported in 1 donor each in the worldwide survey of LDLT programmes (n=71centres)[9].

Myocardial infarction was reported in 3 donors in the worldwide survey of LDLT programmes (n=71 centres)[9].

Cardiac failure was reported in 1 donor in the survey of living donors (n=3565) in 38 Japanese LDLT centres[12].

Gastro-oesophageal reflux (associated with left liver hypertrophy)

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[17].

Aborted hepatectomy events (defined as any procedure stopped after the donor entered the preoperative area).

Aborted hepatectomy was estimated to have occurred in 1% (136/11,553) of procedures on donors in the worldwide survey of LDLT programmes (n=71 centres)[9]. 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 ($p<0.001$)[9].

Validity and generalisability of the studies

- There is variation in donor operative techniques (right and left lobe hepatectomy, and segmentectomy). In some studies, there were differences between the basic characteristics of patients treated with living-donor liver transplantation and patients treated with cadaveric liver transplantation.
- Some studies also included recipients with hepatocellular carcinoma.
- There is a possibility of study population overlap and duplicate publication.
- Most of the literature is from outside the UK such as Japan, Korea and Hong Kong. The results from these studies may not be fully applicable to European patient populations because of differences in the indications case-mix and the potential for biological differences affecting graft survival or rejection.
- Donor quality of life and psychological outcomes are only reported in a few papers.
- Few studies used validated measures for donor outcomes, and most focused on immediate complications, with fewer looking at long-term outcomes. However, given regeneration of liver tissue in donors, focusing on relatively short-term outcomes may be appropriate.
- Donor mortality appears to be consistent (0.2%) between studies.
- Few studies included details of centre experience. Results from larger centres may not be generalisable to smaller centres.
- Some single-centre-specific studies have reported higher morbidity; but these adverse events were generally not severe (see appendix A).
- Most data are from registries worldwide.

Existing assessments of this procedure

Four reviews were identified on living-donor liver transplantation (both recipient and donor outcomes):

- Alberta Heritage Foundation for Medical Research (2004) Living donor liver transplantation in children. Information Paper IP21. Edmonton, Canada: Alberta Heritage Foundation for Medical Research.

- Alberta Heritage Foundation for Medical Research (2004) Adult to adult living donor liver transplantation. TN45 TechNote. Edmonton, Canada: Alberta Heritage Foundation for Medical Research.
- Middleton P, Duffield M, Lynch S et al. (2003) Live donor liver transplantation adult outcomes: a systematic review. ASERNIP-S Reports Nos 22 and 34. Stepney, South Australia: Australian Safety and Efficacy Register of New Interventional Procedures – Surgical.
- Middleton PF, Duffield M, Lynch SV et al. (2006) Living donor liver transplantation – adult donor outcomes: a systematic review. Liver Transplantation 12: 24–30.

This overview includes 3 of the above reviews[1,5,11].

The systematic review that assessed the safety of LDLT for the donor concluded that 'there is some risk of mortality and morbidity for LDLT donors, and the long-term risks are unknown'. The authors recommended that strict guidelines are necessary for the performance of adult-to-adult LDLT, in particular with respect to the process of LDLT donor selection, and contraindications for donor selection, and to the process of listing potential LDLT recipients. Additionally, the authors acknowledged the poor evidence available for LDLT, and suggested that all LDLT procedures need to be submitted to a registry[11].

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Living-donor lung transplantation for end-stage lung disease. NICE interventional procedure guidance 170 (2006). Available from http://www.nice.org.uk/guidance IPG170

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to where comments are

considered voluminous, or publication would be unlawful or inappropriate. Seven Specialist Adviser Questionnaires for living donor liver transplantation were submitted and can be found on the NICE website [https://www.nice.org.uk/guidance/indevelopment/GID-IP2800].

Specialist advice sought from consultants who have been nominated or ratified by their Specialist Society or Royal College in 2006 is summarised below.

Mr John Buckels, Professor J Garden, Mr N Heaton, Mr David Mayer, Professor Millar, Professor Neuberger, Mr C Rudge and Mr Mark Stringer

- The majority of Specialist Advisers considered that living-donor liver transplantation is an established procedure for people, particularly children, with end-stage liver disease. However, there are still some uncertainties around long-term survival and graft function in comparison with cadaveric liver grafts.
- Adult-to-adult living-donor liver transplantation is associated with greater risk than adult-to-child transplantation for both the donor and the recipient.
- The Specialist Advisers considered biliary and vascular complications to be the main complications following living-donor liver transplantation.
- With respect to donors, the Specialist Advisers expressed concerns about donor risk. It was noted that donor mortality varied depending on the size of the liver transplanted, with right hepatectomy possibly associated with increased risk to the donor. Other complications following donor hepatectomy listed by the Specialist Advisers included liver failure, bile leaks, infection and haemorrhage.
- A key issue is donor risk – there have also been several documented deaths – as well as possibility that donors will need transplantation themselves.
- Left lateral segment liver donation from parent to child is not controversial but the practice of adult-to-adult living-donor liver transplantation (using the right lobe) is still regarded as controversial.
- The greater the extent of liver resection required for donation the greater the risk.
- Overall results for the recipient following living-donor transplantation appear to be no better than with current cadaveric grafts.

- There is some concern that there is a tendency to consider patients for living-donor liver transplantation despite their not meeting criteria for cadaveric transplantation (for example, patients with carcinoma).
- There is some suggestion that failures and deaths are not always reported in the literature (publication bias).
- There is no coordinated registry.
- The evidence suggests that high-volume transplant centres have better outcomes.
- Transplantation should be performedin units with adequate experience.
- Only a small number of patients would be eligible for this procedure in the UK.

Audit criteria

Specialist Advisers suggested some of the following audit criteria:

- Survival
- Survival on waiting list
- Graft survival
- Immunosuppression requirements
- Retransplantation rates
- Complications (recipient)
- Quality of life (recipient and donor)
- Donor morbidity and mortality
- Impact on occupation/work (donor)

Patient commentators' opinions

NICE's Public Involvement Programme sent 60 tailored and differentiated questionnaires to 1 NHS trust for distribution to both donors and recipients of living-donor liver transplantation, 30 for each group of donors/recipients. NICE received 26 completed questionnaires; 50% (15/30) from donors and 37% (11/30) from recipients.

While all donors said that the procedure had a positive effect on them (mainly emotionally), a significant majority told us that there were also a number of mainly short-term negatives coping with the physical and emotional impact after the operation. However, the short-term negatives must have been outweighed by the long-term positives because 100% would recommend the procedure. A substantial majority said that they had received adequate counselling.

All patients who responded said that the procedure had a positive effect on them and that they would recommend it to others. However, nearly half of the patients said it also had negative effects on them.

Issues for consideration by IPAC

- One of the main issues would seem to be the use of right lobe liver grafts. Few publications have looked at donor complications following right lobe donation and long-term outcomes of recipients after right lobe transplantation.
- Because of the large volume of literature, a safety filter was applied to the literature search (see appendix C). It is possible that this excluded potentially relevant articles. However, some of this potential risk should have been mitigated by the inclusion of systematic reviews.
- In the UK, NHSBT UK transplant registry collects data on all liver transplantations performed within the NHS, including paediatric living-donor liver transplants. Since 1993, 296 liver transplants from living donors have been performed in the UK; 93% (277/296) from living related donors, 6% (17/296) from living unrelated donors and 1% (2/296) from altruistic donors. In 2013–14, there were 18 adult-to-adult living donor liver transplants and 14 adult-to-child living-donor liver transplants. This includes some overseas patients. In 2013, 1 donor had a ‘super urgent’ liver and kidney transplantation as a direct result of donation and is recovering slowly.
- In the USA, the United Network for Organ Sharing has developed a similar database that contains data on every organ donation and transplantation event in the USA since 1986.

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5. Middleton P, Duffield M, Lynch S et al. (2003) Live donor liver transplantation adult outcomes: a systematic review. ASERNIP-S Reports Nos 22 and 34. Stepney, South Australia: Australian Safety and Efficacy Register of New Interventional Procedures – Surgical.
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7. Olthoff KM, Merion RM, Ghobrial RM et al. (2005) Outcomes of 385 adult-to-adult living donor liver transplant recipients: a report from the A2ALL Consortium. Annals of Surgery 242: 314–23.
8. Hwang S, Lee SG, Sung KB et al. (2006) Long-term incidence, risk factors, and management of biliary complications after adult living donor liver transplantation. Liver Transplantation 12: 831–8.
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15. TakadaY, Suzukamo Y.et al (2012). Long-term quality of life of donors after living donor liver transplantation. Liver Transplantation 18: 1343-1352.

16. Zhang S, Dong Z.et al (2011). Right lobe living-donor liver transplantation with or without middle hepatic vein: A meta-analysis Transplantation Proceedings 43: 3773-3779

17. Sotiropoulos GC, Radtke A et al (2011). Long-term follow-up after right hepatectomy for adult living donation and attitudes toward the procedure. Annals of surgery 254:694-701.

18. Nadalin S, Malago M et al (2006). “Hepar Divisum”- As a rare donor complication after intraoperative mortality of the recipient of an intended living donor liver transplantation. Liver transplantation 12: 428-434.

Appendix A: Additional papers on living-donor liver transplantation

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	**Number of patients/follow-up**	**Direction of conclusions**	**Reasons for non-inclusion in table 2**
Abbasov PA, Iylmaz S et al (2014). Evaluation of postoperative complications in liver donors in accordance with Clavien classification]. Klin.Khir. (5) 32-34.	Retrospective analysis n=250 donors LDLT	Clavien classification was used for estimation of the postoperative complications severity. There was established, that hepatic transplantation from a living donor constitutes a secure procedure, which is effective in treatment of hepatic diseases in terminal stage.	Larger studies included in table 2.
Adcock L, Macleod C, Dubay D, et al (2010). Adult living liver donors have excellent long-term medical outcomes: the University of Toronto liver transplant experience. Am J Transplant. 10:364-371.	Prospective case series (retrospective chart review) 2000-2008 Canada n=202 adults RL-LDLT Follow-up: mean donor follow-up was 33.9 months.	Donor survival was 100%. Overall donor complication was 41% (39.6% of donors experienced grade 1-3 complications during the first year after surgery and 3 donors had complications after 1 year). All donors returned to predonation employment or studies and 2% (n=4) donors has psychiatric complications.	Similar studies included in table 2.
Azzam A, Uryuhara K et al (2010). Analysis of complications in hepatic right lobe living donors. Annals of Saudi Medicine. 30: 18-24	Retrospective case series n=311 donors RH-ALDLT (284 without MHV and 27 with MHV) Japan (single centre) 1998-2003 Follow-up: 7 years	1 donor died of liver failure due to small residual liver volume (26%) and steatohepatitis. Complications occurred in 33.4% (104/311) donors- 123 complications. Donors had 1 or more complications- grade I in 57.7% (n=71), grade II 7.3% (n=7), grade II a 31.7% (n=39) grade IIIb 2.5% (n=3), grade IV 0.8% (n=1). Biliary complications were the most common 12% (37/311).	RL-ALDLT Similar studies included in table 2.

Beavers KL et al (2001). The living donor experience: donor health assessment and outcomes after living donor liver transplantation. Liver transplantation. 17:943-947.	Survey USA (single centre) 1996-2000 n=27 (Adult to adult n=14) LDLT Follow-up: mean 13 months	64% reported immediate complications; complications requiring readmission were reported by 29%. Mean time to recovery was 18 weeks (range 1-52 weeks). No significant change was reported in physical, social activity or emotional stability and 92% of donors resumed their pre-donation occupation. 100% of donors stated that they would donate again and recommend to someone in contemplation.	Similar studies included in table 2.
Beavers KL, Sandler RS et al (2003). Donor morbidity associated with right lobectomy for living donor liver transplantation to adult recipients: a systematic review. Liver Transplantation, 8:110-117.	Systematic review USA n=12 studies (1151 donors) Right lobectomy for LDLT Varied follow-up	Morbidity ranged from 0-67%. Bile leaks, prolonged ileus and minor wound problems were the most commonly reported complications. Other complications include neuropraxia, transient pressure sores, pleural effusions, edema, and atelectasis. 2 deaths were reported. Average length of hospital stay was 9.9days.	Similar studies included in table 2.
Belghiti J, Liddo G et al (2012). "Inherent limitations" in donors: control matched study of consequences following a right hepatectomy for living donation and benign liver lesions. Annals of Surgery 255: 528-533	Prospective non-randomised comparative study France (single centre) n=32 RH for benign lesions versus 32 RH for LDLT.	RLV on postoperative day 7, was similar between the 2 groups resulting in significantly higher regeneration rate in LD group 89% vs 55%, p=0.009). Overall complication rate was lower in the benign lesion group than living donors (46% vs 21%, p=0.035).	Impact of RL-ALDLT compared with RH for benign lesions.

Broelsch CE et al (2000). Living donor liver transplantation in adults: outcomes in Europe. Liver transplantation. 6, 2:S64-65.	Survey n=123 adults LDLT in 11 centres in Europe Study period not reported.	70% donors experienced no complications. Minor complications occurred in 14% but 17.8% (22/123) patients experienced major complications. There was 1 (0.8%) donor death from multiple postoperative complications.	Similar studies included in table 2.
Broering DC, Wilms C, Bok P et al. (2004) Evolution of donor morbidity in living related liver transplantation: a single-center analysis of 165 cases. Annals of Surgery 240: 1013–24.	Donor 165 patients. FU: unclear. 1991–2003	One early donor death was observed. Morbidity also decreased with increasing experience.	Similar studies included in table 2.
Campsen J. et al. Outcomes of Living Donor Liver Transplantation for Acute Liver Failure: The Adult-to-Adult Living Donor Liver Transplantation Cohort Study. Liver Transplantation 14:1273-1280	Retrospective and prospective cohort study n=13 acute liver failure patients and their donors from adult to adult LDLT cohort. LDLT 1998-2007 USA	50% (5/10) of living donors experienced 7 complications. This is comparable to the rate of complications by all donors in the A2ALL study of 37.7%. Donor perioperative survival was 100%. 70% recipients survived.	LDLT in selected patients with acute liver failure and outcomes of their donors.
Chan SC, Fan ST et al (2007). Effect of side and size of graft on surgical outcomes of adult-to-adult live donor liver transplantation. Liver Transplantation 13: 91-98.	Prospective comparative case series 1996-2007 China RL ALDLT (n=29) versus LL ALDLT (n=16)	Postoperatively, left lobe liver donors had significantly lower international normalised ratios and serum total bilirubin and no complications. 7% complications (2 wound infections) were seen in RL donors.	Effect of RL and LL LDLTs of comparable size and donor outcomes.
Chan SC, Liu CL et al (2006). Donor quality of life before and after adult-to-adult right liver live donor liver transplantation. Liver Transplantation.12: 1529-1536	prospective case series China 2002-2003 n=30 donors RL-A-A LDLT Follow-up: median1 year	No donor mortality or major complications. Donor QOL worsening was most significant in the first 3 postoperative months, particularly among physical components. The physical and mental components returned to previous levels in 6-12 months though the Karnofsky performance scores were lower at 1 year (p=0.011). 86.7% (26/30) said they would donate again. Older adults were unwilling to donate again.	QOL
Chan KL, Fan ST.et al (2009). Pediatric liver transplantation in Hong Kong-a domain with scarce deceased donors. Journal of Pediatric Surgery. 44: 2316-2321	Case series n=78 paediatric patients (n=62 live donors, 21 deceased donors) Follow-up:6.5 years	1 live donor developed temporary peroneal palsy, an another developed lung collapse (3%, 2/620. All live donors resumed their normal activities with no difficulty.	LT for paediatric patients.
Cho JY, Suh KS et al (2006). Mild hepatic	Prospective case series	No mortality or hepatic failure observed, no reoperation, or	Impact of mild hepatic steatosis

steatosis is not a major risk factor for hepatectomy and regenerative power is not impaired. Surgery. 139: 508-515	Korea 2002-2003 n=54 donors with mild hepatic steatosis (group 1 <5% MHS, n=36; group 2 5-30% MHS, n=18) LDLT-RH, LH, LLS Follow-up: at least 1 year	intraoperative transfusion needed. LFTs, major and minor morbidities were comparable. Postoperatively liver spleen ratio and liver attenuation index increased rapidly in group 2. No difference in liver regeneration rate at 1 year (p=.4).	on the regeneration rate and changes in remnant liver after hepatectomy in setatotic livers.
Cho EH, Suh KS et al (2007). Safety of modified extended right hepatectomy in living liver donors. Transplant International.20: 779-783	Retrospective comparative case series Korea (single centre) 2002-2005 RH-ALDLT modified extendable RH group, n=18 donors versus conventional RH, n=37 donors Follow-up: 4 months	No mortality occurred. No reoperation or intra-operative transfusion performed. No differences in operative time, blood loss, postoperative hospital stay between the groups (p>0.05). no difference in complication rate between the groups (11 vs 23, p>0.05). the regeneration rate of remnant liver after modified RH and conventional RH were similar (209.8% vs 200% at 4 months, p>0.05).	Safety of modified RH compared with conventional RH in ALDLT.
Cuomo O, Ragozzino A et al (2006). Living donor liver transplantation: early single-center experience. Transplantation Proceedings 38 (4) 1101-1105.	Retrospective case series 2001-2005 Italy n=8 Right lobe LDLT Follow-up: median 24 months	All donors survived. Complications were experienced by 25% (2/8) donors: temporary radial neuropraxia recovered after long term physiotherapy in 1, bile leak from the cut surface of the liver with subphernic collection and symptomatic right pleural effusion, requiring percutaneous catheter drainage, drug related hepatitis in 1.	Similar studies included in table 2.
Dayangac M, Taner CB et al (2011). Utilization of elderly donors in living donor liver transplantation: when more is less? Liver Transplantation. 17: 548-555	Retrospective comparative case series n=150 2004-2009 Turkey LDLT (RH with MHV or RH with RLV <35%) using older donors. Group 1 (donor aged>50 years, n=28) vs group 2 (donor aged <50 years, n=122). Recipients who had a graft from these donors. Follow-up: median 41 months	Donor outcomes: No death or grade 4 complications. Overall and major complications were similar in the 2 donor age groups (28.6% and 14.3% in group 1 and 32% and 8.2% in group 2, p=0.8, 0.2 respectively) There was significant correlation between the type of surgery in donors and major complication rate in older donors.	Impact of age of donors on donor outcomes and impact of RL hepatectomy.

Dondero F, Taille C, Mal H et al. (2006). Respiratory complications: a major concern after right hepatectomy in living liver donors. *Transplantation* 81: 181–6.	Donor –right lobecotomy 112 donors. 1998–2003.	9.8% of donor developed serious respiratory complications.	Only looked at respiratory complications.
El-Serafy , Kassem, AM et al (2009). Quality of life of Egyptian donors after living-related liver transplantation. Arab Journal of Gastroenterology. 10: 21-24	Egypt 2001-6 Retrospective comparative case series n=30 LDLT donors vs 30 healthy volunteers (control) Quality of life + SF-36 v2 at mean 3.28 years after donation.	None of the donors required re-surgery and no deaths were reported. 13.3% (4/30) donors had minor complications, which did not affect their quality of life and had no long term effects. No significant difference between donors and control group noted when means of physical, mental component summary were compared. The physical functioning domain shoed a statistically significant difference between the groups. All donors returned to regular activities within 2-4 months post donation.	Similar studies included in table 2.
Egawa H, Inomata Y, Uemoto S et al. (2001) Biliary anastomotic complications in 400 living related liver transplantations. *World Journal of Surgery* 25: 1307.	Mixed (child and adult) 391 patients. FU: unclear. 1990–1998	Overall incidence of biliary complications was 18%.	Similar studies included in tables 2 and 3.

Egawa H, Uemoto S, Inomata Y et al. (1998) Biliary complications in pediatric living related liver transplantation. *Surgery* 124: 901–10.	Children 205 patients. FU: unclear. 1990–6	Incidence of bile complications was 13.9%.	Only looking at complications. Similar studies included in table 2.
Fujita S, Kim ID, Uryuhara K et al. (2000) Hepatic grafts from live donors: donor morbidity for 470 cases of live donation. *Transplant International* 13: 333–9.	Donor 470 donors. FU: Mean 1 month. 1990–1999	Biliary leakage was the most common complication. No mortality noted.	Article was about donor morbidity – similar articles included in table 2.
Fernandes R, Pacheco-Moreira LF, Enne M, et al (2010). Surgical complications in 100 donor hepatectomies for living donor liver transplantation in a single Brazilian center. Transplant Proc. 42:421-423.	Retrospective medical chart review Brazil (single centre) 2002-2008 LDLT n=100 donors (57 for adult transplants and 43 for paediatric transplants) 49 right, 2 left and 49 left lateral segmentectomies. Follow-up: median 39.6 months	None of the donors had life-threatening complications or died. 28 complications observed in 26 donors. According to Clavien scoring system, Grade I complications (n=11, 39.2%), grade II (n=8, 28.5%) grade III n=9, 32.3%). No grade IV or V, most common complication was a biliary tract injury.	Similar studies included in table 2.
Fong YK, Chan SC et al (2013). Remnant left liver size and recovery of living right liver donors. Hepatology International.7: 734-740.	Prospective case series China 1996-2010 n=349 donors RL LDLT cohort divided into 9 subgroups based on RLLV (<30 to >47.5)	Complication rates ranged from 0-75%, rate of grade 3 or above complications ranged from 0-3.8%. Donors with smaller RLLV had a high risk of complications. Slow recovery was associated with smaller RLLV in RL. Donors with smaller RLLV had a higher level of serum bilirubin and PT after surgery.	RL donor outcomes based on remnant liver volume.
Facciuto M, Contreras-Saldivar A et al (2013). Right hepatectomy for living donation: role of remnant liver volume in predicting hepatic dysfunction and complications. Surgery 153: 619-626.	Retrospective review USA 1999-2010 n=137 donors RH-ALDLT	25% (32/137) donors developed postoperative hepatic dysfunction, RLV did not predict postoperative liver dysfunction (p=.9) but it was associated with peak INR (p=.04). 33% donors (45/137) had complications, 42% donors whose RLV<30% experienced complications compared to 31% of donors whose RLV is >30% (p=.3). cell saver utilisation and AST levels were associated with complications. 1 death due to gas gangrene of stomach.	RH donor outcomes based on remnant liver volume.

Ghobrial, RM, Freise CE, Trotter JF, et al (2008). Donor morbidity after living donation for liver transplantation. Gastroenterology. 135:468-476.	Retrospective observational study USA 9 centres 1998-2003 n=405 donors A-A LDLT Follow-up : median 6 months (range 5 days-5.6 years)	Overall complication rate 38%. 27% had grade I (n=106) and 26% had grade II (n=103) grade III (2%, n=8), grade 4 0.8% (n=3). Common complications include biliary leaks, bacterial infections, incisional hernia (n=22, 6%), pleural effusion requiring intervention (n=21, 5%), neuropraxia (n=16, 4%), re-exploration, wound infections (n=12, 3%), intra-abdominal abscess (n=9, 2%), 2 had portal vein thrombosis, 1 had inferior vena caval thrombosis.	Similar multicentre consortium studies included in table 2.
Gokce S, Durmaz O et al (2011). Assessment of living donors with respect to pre- and posttransplant psychosocial properties and posttransplant family functioning in pediatric liver transplantation. Turkish Journal of Gastroenterology. 22: 36-41	Retrospective review Turkey (single centre) 1999-2007 LDLT n=32 donors recipients- paediatric patients Follow-up: median 27 months	19.3% 95/32) had anxiety about postoperative complications and QOL. Return to work and feeling of complete wellbeing were accomplished at a median of 4 weeks and 10 weeks.43.4% 914/32) donors reported pain around incision and non-specific GI problems postoperatively. 25% (8/32) had psychological problems. -2 had depression needing drug or psychotherapeutic intervention. 34.6% (9/32) displayed nervous behaviour towards their spouses, 2 (7.7%) divorced. Life of other family members were negatively affected in 8 (30.7%). 2 donor spouses failed to carry out domestic responsibilities.	clinical, QOL-psychosocial and family functioning outcomes reported in donors

Grewal HP, Thistlewaite JR, Jr, Loss GE et al. (1998) Complications in 100 living-liver donors. *Annals of Surgery* 228: 214–19.	Donor 100 patients. FU: unclear. 1989–96	Minor complications occurred in 20% of patients.	Similar studies included in table 2.
Hori T, Kirino I, and Uemoto S (2015). Right posterior segment graft in living donor liver transplantation. Hepatol.Res.	Retrospective case series n=14 LDLT with right posterior segment graft (RPSG).	Donors' postoperative courses were uneventful. To adjust diameters and lengths between grafts and recipients, dual anastomoses for PV reconstruction and graft interpositions for PV and HA reconstruction were required in one case each. HA thrombosis occurred in two cases and PV thrombosis in one. Biliary complications occurred in two cases. Though there was no significant difference in survival following RPSG versus other grafts, critical complications were observed in recipients. The RPSG is a useful option in LDLT. However, careful consideration is required for RPSG harvest and LDLT performance, both before and during surgery.	Larger studies included in table 2.
Hwang S, Lee SG et al (2006). Lessons learned from 1,000 living donor liver transplantations in a single center: how to make living donations safe. Liver Transplantation. 12: 920-927	Retrospective case series 1996-2010 Asia, South Korea (single large centre) n=827 donors LDLT- A-A (N=697) A-P (n=130) right lobe-690	No donor mortality. 10% (83/827) had complications. Wound complications most common 5.8% (n=48), Grade 1 in 56, grade 2 in 2, grade 3a in 15, grade 3b in 10 donors. Surgical and interventional management was successful in all grade 3 complications. Biliary complications were higher in younger donors.	Similar studies included in table 2.
Hwang S, Lee SG, Joh JW et al. (2005) Liver transplantation for adult patients with hepatocellular carcinoma in Korea: Comparison between cadaveric donor and living donor liver transplantations. *Liver Transplantation* 11: 1265–72.	Adult 312 patients. FU: 3 years. 1992–2002	Living donation can achieve acceptable survival in HCC patients.	Only looking at patients with HCC.
Hashikura Y, Kawasaki S, Terada M et al. (2001) Long-term results of living-related donor liver graft transplantation: a single-center analysis of 110 transplants.	Mixed (adult and child) 110 patients. FU: unclear. 1990– 1999	The 1-, 3- and 5-year actuarial patient survival rates were 88%, 85% and 85%, respectively.	Similar studies included in tables 2 and 3. Difficult to differentiate between child and adult patients.

Transplantation 72: 95–9.			
Hashimoto T, Sugawara Y, Kishi Y et al. (2005) Long-term survival and causes of late graft loss after adult-to-adult living donor liver transplantation. *Transplantation Proceedings* 37: 4383–5.	Adult 176 patients. FU: 33 months. 1996–2004	3- and 5-year survival rates were 95% and 90%, respectively.	Limited information.
Ibrahim S, Chen CL et al (2006). Small remnant liver volume after right lobe living donor hepatectomy. Surgery. 140: 749-755	Retrospective review Taiwan (single centre) 1999-2004 n=86 RL donors RL LDLT Group 1 (<30% remnant liver volume, n=8) Group 2(>30% liver volume, n=78)	There were no differences in donor characteristics, types of graft, operative parameters, and post-operative liver and renal function as well as liver volume at 6 months post-donation between the 2 groups. The overall donor complication rate was 6.98%, and all complications occurred in group 2 donors.	RL donor outcomes based on remnant liver volume.
Inomata Y, Tanaka K, Uemoto S et al. (1999) Living donor liver transplantation: an 8-year experience with 379 consecutive cases. *Transplantation Proceedings* 31: 381.	Donor 379 patients. FU: unclear. 1996–2002	There was no mortality or permanently remaining complications.	Limited information.
Jiang XZ, Yan LN et al (2008). University of California at San Francisco criteria can be applied to living donor liver transplantation for hepatocellular carcinoma: single-center preliminary results in 27 patients. Transplantation Proceedings. 40: 1476-1480	Retrospective case series n=29 donors, 27 recipients with HCC A-A LDLT 2002-2006 China Follow-up: 5 years	Overall complication rate was 17.2%. 2 had major complications including intra-abdominal bleeding and portal vein thrombosis.3 had minor complications: wound steatosis, pleural effusion, and transient chyle leakage. No donor mortality reported. All donors recovered and returned to earlier occupations.	Similar studies included in table 2.
Kashyap R, Ryan C et al (2009). Liver grafts from donors with central nervous system tumors: A single-center perspective. Liver Transplantation.15: 1204-1208.	Retrospective review 1992-2006 USA (single centre) 42 donors with CMS tumour (32 malignant, 10 benign) Follow-up: mean 29 months	One donor died (she had a juvenile pilocytic astrocytoma of the cervical spine with metastasis to brain. She died of intracranial haemorrhaging.	Donors with CNS tumours. Study mainly reports recipient outcomes.
Kim SH and Kim YK (2013). Upper midline incision for liver resection. HPB. 15: 273-278	Retrospective case series South Korea 2006-2010 n=308 liver resections (of which 148 living	Total complications 6.8% (n=10) in living donors. Grade I 2.7% (4), grade II 91.4%, n=2), grade III 2.7% (n=4).	Newer modified technique for resection.

	donors) Upper midline incision for liver resection. Follow-up: median 31 months.		
Kiuchi T, Inomata Y, Uemoto S et al. (1997) Living-donor liver transplantation in Kyoto, 1997. *Clinical Transplants* 191–8.	Mixed (adult and child) 74 patients. FU: unclear. 1996–1997	Graft and patient survival rates during the past 12 months were 81.3% and 82.4%, respectively.	Limited outcomes reported. Similar studies included in tables 2 and 3.
Lee SY, Ko GY, Gwon DI et al. (2004) Living donor liver transplantation: complications in donors and interventional management. *Radiology* 230: 443–9.	Donor 386 patients. FU: unclear. assumed mean 38 weeks (range 18-64 weeks) 1997–2001	No donor deaths occurred. There were 56 complications in 52 donors -41 (18.9%) right lobe and 11 (7.0%) left lobe – overall complication rate of 13.5%. Authors noted that in most donors, prolonged abnormal liver function was a sign of a postoperative complication such as a biliary stricture or portal vein stenosis.	Similar studies included in table 2.
Lei J, Yan L et al (2013). Donor Safety in Living Donor Liver Transplantation: A Single-Center Analysis of 300 Cases. PLoS ONE.8 (4) .Article Number: e61769.Date of Publication: 25 Apr	Retrospective case series n=300 (first 5 years n=129; later 5 years n=154) 2002-2012 China (single centre) LDLT Follow-up: average 45 months	No donor mortality. overall morbidity 25.3% Complications were either grade I or II. Fewer complications in the later period (n=34) than the initial period (n=42) (19.9% vs 32.6%, p<0.001). Biliary complications most common 9%.2 donors had grade 3 complications. 8 years after surgery 22 donors showed lower platelet levels compared with preoperative levels. 98.4% donors returned to previous levels of social activity and work and 99.2% of them would donate again if needed.	Similar studies included in table 2
Lei JY, Yan LN et al (2012). Donor morbidity including biliary complications in living-donor liver transplantation: a single centre analysis of 283 cases. Transplantation. 94:e51-52.	Retrospective case series n=283 LDLT		Similar studies included in table 2
Li F, Yan L et al (2007). Complications in the right lobe adult living donor: single-center experience in China. Transplantation Proceedings. 39: 2977-2980	Retrospective review n=62 donors USA (single centre) 2002-2006 RL-ALDLT Follow-up: mean 16 months	Overall complication rate was 29% Complications included pleural effusion (9.6%, n=6), bile leaks (4.8%,n=3), wound infection (3.2%, n=2), pneumonia (3.2% , n=2), chyle leak (1.6%, n=1), intra-abdominal bleeding (1.6%, n=1), sub phrenic effusion (1.6%,n=1), portal vein thrombosis (1.6%, n=1) and	RL-ALDLT Similar studies included in table 2.

		chylothorax (1.6%, n=1). No donor mortality.	
Li C, Mi K.et al (2011). Outcome comparison of right hepatectomy for living liver donation versus for hepatic patients without cirrhosis. Journal of Gastrointestinal Surgery. 15: 982-987	Retrospective comparative case series n=120 (Group A 60 LDLT donors versus Group B, 60 normal liver hepatic patients).	Postoperatively group A had more intraoperative bleeding but the amount of blood transfusion was similar between the groups. Overall postoperative surgical morbidity was 31.7% for group A and 35% for group B (p=0.699). The total bilirubin level and coagulation functions of group A were worse than group B during early postoperative period.	Outcomes of LDLT donor compared with hepatic patients with a normal liver.
Li C, Wen TF et al (2012). Safety of living donor liver transplantation using older donors. Journal of Surgical Research.178: 982-987.	Retrospective comparative case series 2005-2009 China LDLT using older and younger donors. Group A (donor aged>50 years, n=21) vs group B (donor aged <50 years, n=108). Follow-up: mean 45.6 months.	Donor outcomes: No death. Overall complications 30.2% (39/129). Complication rates were 38.1% and 28.7% for group A and B donors (p=0.719).	Effect on outcomes for donors and recipients who received a graft from older donors.
Lin CC, Chuang FR, Wang CC et al. (2004) Early postoperative complications in recipients of living donor liver transplantation. *Transplantation Proceedings* 36: 2338–41	Mixed (adult and child) 140 patients. FU: 3 months. 1994–2003	Surgical complications requiring re-laparotomy occurred in 7.9% of patients.	Similar studies included in tables 2 and 3.
Liu B, Yan LN et al (2007). Clinical study on safety of adult-to-adult living donor liver transplantation in both donors and recipients. World Journal of Gastroenterology.13: 955-959.	A-A LDLT 2002-2006 China (single centre) 50 recipients 52 living donors (49 RL without MHV, 3 LL)	All donors' remnant liver volume was over 35% of the whole liver volume. No donor mortality. All are well and returned to daily life and work. Complications included transient chyle leakage, portal venous thrombosis, sub-phrenic effusion, pleural effusion.	Outcomes of donors and recipients in A-A LDLT using RL without MHV.
Lo CM, Fan ST, Liu CL et al. (2004) Lessons learned from one hundred right lobe living donor liver transplants. *Annals of Surgery* 240: 151–8.	Adult – right lobe only 100 patients. FU range: 7–79 months.	There is a learning curve in adult right lobe.	Similar studies included in table 3.
Marsh JW, Gray E, Ness R, Starzl TE (2009). Complications of right lobe living donor liver transplantation. J Hepatol. 51:715-724	Retrospective review 2003-2006 USA (single centre) n=121 donors and recipients	Donors: All donors survived. 20% complication rate in donors. 10.7% (13/121) donors had grade 3 (n=9) or IV (n=4) complications of which 5 were	RL-ALDLT Similar studies included in table 2.

	RL-ALDLT Follow-up: limited to first year	graft related.	
Miller CM, Gondolesi GE, Florman S et al. (2001) One hundred nine living donor liver transplants in adults and children: a single-center experience. Annals of Surgery 234: 312.	Case series Mixed (adult and child)109 patients. 1993–1998 FU: unclear.	Survival at 1 year was 89.9% in children and 85.6% in adults.	Similar studies included in tables 2 and 3.
Morioka D, Egawa H et al (2007). Outcomes of adult-to-adult living donor liver transplantation: a single institution's experience with 335 consecutive cases. Annals of Surgery. 245: 315-325	Retrospective case series Japan 1994-2003 n=332 donors A-A LDLT Follow-up: 53 months	Overall complications in donors 39.7% (133/332). 60 had major complications, most frequent complication was bile leakage, n=39,next frequent was pulmonary embolism in 5/332 and depression reported in 2/332. No mortality and all donors leading normal daily lives. Factors impacting donor outcomes were also reported. Graft type and experienced had a significant impact on surgical outcomes of donors.	Similar studies included in table 2.
Moss J, Lapointe-Rudrow D et al (2005). Select utilization of obese donors in living donor liver transplantation: Implications for the donor pool. American Journal of Transplantation.5: 2974-2981.	Retrospective comparative case series 1999-2003 USA (single centre) n=68 donors (BMI<30, 52 VS BMI >30, 16) A-ALDLT Follow-up: median 25 months for both groups	Postoperative complications in donors included wound infection, pneumonia, hernia, fever, ileus, biliary leak, biliary stricture, thrombosis, bleeding, hepatic dysfunction, thrombocytopenia, deep vein thrombosis, pulmonary embolism, difficult to control pain, depression and anxiety. The incidence of wound infection increased with BMI, 4% for BMI<30 and 25% for BMI>30 (p=p.024). No statistically significant differences for all other complications. No donors died.	Data on obese donors.
Nagai S, Fujimoto Y et al (2009). Mild hepatic macrovesicular steatosis may be a risk factor for hyperbilirubinaemia in living liver donors following right hepatectomy. British Journal of Surgery. 96: 437-444	Retrospective case series (review of medical records) n=41 donors RH-LDLT Group 1 (n=10 with mild hepatic macrovesicular steatosis) versus Group 2 (n=31 with normal livers)	The median duration for normal total bilirubin level was 14 and 5 days in group 1 and 2 (p=0.028). The total peak bilirubin level was higher in group 1 than 2 (80.4 vs 49.6mmol, p=0.033). 8 donors in group 1 and 13 in group 2 had at least 1 complication. No donor had grade III to V complication. All donors returned to daily life activities. MHS is an independent risk factor for hyperbilirubinemia (p=0.034).	Impact of mild hepatic steatosis on donor outcomes after right hepatectomy
Olthoff, K. M., Abecassis, M. M et al (2011). Adult-to-Adult Living Donor Liver	Cohort Study (A2ALL) 9 A2ALL centers (n =	No significant difference in overall mortality between A2ALL and non-A2ALL centers	defines risk factors for patient mortality and graft

Transplantation Cohort Study Group. Liver Transplantation 17 (7) 789-797.	702) and 67 non-A2ALL centers (n = 1664) 1998 - 2007 Scientific Registry of Transplant Recipients database analysed	was found. Higher hazard ratios were associated with donor age (HR = 1.13 per 10 years, P = 0.0002), recipient age (HR = 1.20 per 10 years, P = 0.0003), serum creatinine levels (HR = 1.52 per loge unit increase, P < 0.0001), hepatocellular carcinoma (HR = 2.12, P<0.0001) or hepatitis C virus (HR = 1.18, P = 0.026), intensive care unit stay (HR = 2.52, P< 0.0001) or hospitalization (HR = 1.62, P < 0.0001) versus home, earlier center experience (LDLT case number 15: HR = 1.61, P < 0.0001, and a cold ischemia time >4.5 hours (HR = 1.79, P = 0.0006). Except for center experience, risk factor effects between A2ALL and non-A2ALL centers were not significantly different. Study	loss in living donor liver transplantation (LDLT)
Oshita A, Tashiro H et al (2012). Safety and feasibility of diet-treated donors with steatotic livers at the initial consultation for living-donor liver transplantation. Transplantation 93: 1024-1030.	Non-randomised comparative study Japan Diet treated donors (n=41) versus non-diet treated donors (n=87). Follow-up: post-operative	Surgical outcomes, including postoperative liver function tests, perioperative complications, and liver regeneration rates did not significantly differ between non-diet and diet treated donors.	LDLT assessing differences in diet and non-diet treated donors.
Ozgor D, Dirican A et al (2012). Donor complications among 500 living donor liver transplantations at a single center. Transplantation Proceedings.44: 1604-1607.	Retrospective case series n=500 donors 2007-2011 Turkey LDLT Follow-up: mean 30 months	No donor mortality. 149 complications in 18.6% (93/500) donors: overall incidence of reoperations was 7.2%.most common problems were biliary complications in 7.7%. Grade I 77, II 9, III 27, IIIb 35, IV a 1.	Similar studies included in table 2.
Ozkardesler, S., Ozzeybek, D et al (2008). Anesthesia-related complications in living liver donors: the experience from one center and the reporting of one death. American Journal of Transplantation 8: 2106-2110.	1997 - 2007 Turkey (single centre) Retrospective review n=113 donors Right hepatectomy (resection of segments 5-8) 101 donors, left lobectomy (resection of segments 2-3) in 11 donors, and left hepatectomy (resection of segments 2-4) in 1 donor.	Minor anaesthetic complications were shoulder pain, pruritus and urinary retention related to epidural morphine, and major morbidity included central venous catheter-induced thrombosis of the brachial and subclavian vein, neuropraxia, foot drop and prolonged postdural puncture headache. One of 113 donors died from pulmonary embolism on the 11th postoperative day. This procedure has some major risks related to anaesthesia and surgery.	Safety outcomes and death already covered in table 2.
Ozsoy, M., Unalp, O. V., et al (2014). Results of	Retrospective case series	No donor mortality. Overall complication ate 41.1%	RL-ALDLT Similar studies

surgery-related complications in donors of right lobe liver graft: analysis of 272 cases. Transplantation Proceedings 46: 1377-1383	Turkey (single centre) 2004-2009 n=272 donors RH-ALDLT Follow-up: 5 years	(112/272). Grade I and II complications were observed in 38% (105/272) donors. Most common were fever of unknown origin (20.9%), prolonged hyperbilirubinemia (3.6%). Grade 3 and 4 complications were seen in 2% (6/272) and 1% (3/272- 2 hepatic failure, 1 sepsis) donors. 3 donors had reoperation due to bleeding. Re-laparotomy rate was 1.1%, 1 donor had small bowel perforation and intra-abdominals sepsis secondary to mechanical bowel obstruction. No grade 5 complications.	included in table 2.
Patel S, Orloff M, Tsoulfas G et al (2007). Living-donor liver transplantation in the United States: identifying donors at risk for perioperative complications. Am J Transplant. 7:2344-2349	Retrospective cohort study n=433 (RL and LL LDLT) 2001-2005 13 centres USA (analysis of registry data)	1 perioperative death (0.235) Overall complication ate was 29.1%, and major complication rate was 3.5% grade >3.	Similar studies included in table 2.Study also identified donor risk factors.
Polido W Jr, Hoe LK et al (2007). Acute myocardial infarction after live donor liver surgery. Liver Transplantation. 12:154-156.	Case report n=1 39 year old LDLT donor Singapore, Asia	Died of acute myocardial infarction 10 days after right lobe LDLT.	Death included in Cheah 2012 study in table 2.
Ran S, Wen TF et al (2009). Risks faced by donors of right lobe for living donor liver transplantation. Hepatobiliary and Pancreatic Diseases International.8: 581-585	Retrospective case series China (single centre) 2002-2007 n=105 donors RL-ALDLT Follow-up: at least 6 months	No donor mortality. Major complications occurred in 13.3% (14/105) donors, of whom 3 received conservative treatment, 8 needed invasive paracentesis, and 3 needed further surgery. All donors recovered well and resumed previous occupations.	RL-ALDLT Similar studies included in table 2.

Ringe, B., Xiao, G et al (2008). Rescue of a living donor with liver transplantation. American Journal of Transplantation 8: 1557-1561.	Case report n=1 donor right hemohepatectomy without MHV	4 days later gastric perforation, acute peritonitis was found, gastric repair was performed but patient developed septic shock with acute renal and liver failure. Hepatic function worsened and a liver transplant from a deceased donor was done11 days after right hemohepatectomy. Nine months later the patient is alive, and has fully recovered from his multiple organ failure. According to a review of literature, 4 additional donors who received a liver transplant died. This patient is the only survivor so far.	Deaths due to liver transplantation failure in donors are already covered in Cheah 2012 study in table 2.
Ringe B, Ralph J et al (2007). Death of a living liver donor from illicit drugs. Liver transplantation13:1193-94.	Case report USA Adult to child (lobe unknown) donor had history of substance use.	Died of drug over dose at 57 days.	Death not related to surgery.
Schulz KH, Kroencke S, Beckmann M, et al (2009). Mental and physical quality of life in actual living liver donors versus potential living liver donors: a prospective, controlled, multicenter study. Liver Transpl. 15:1676-1687.	prospective comparative study Germany (single centre) 43 donors versus 33 potential donors (control) LDLT Follow-up: 3 months	Actual donors showed decreased physical QOL, better mental QOL while potential donors were not affected. A decrease in anxiety was found for both groups. The groups did not report a caregiver burden but actual donors showed higher self-esteem.	QOL
Sugawara Y, Makuuchi M, Takayama T et al. (2002) Safe donor hepatectomy for living related liver transplantation. *Liver Transplantation* 8: 58–62.	Donor 130 patients. FU: unclear. 1996–2001	No critical complications were observed. No mortality noted.	Limited outcomes, and many were presented as graphs.
Suh KS, Kim SH, Kim SB et al. (2002) Safety of right lobectomy in living donor liver transplantation. *Liver Transplantation* 8: 910-915.	Donor –right lobecotomy 100 donors. FU: unclear. 1999-2002	There was no mortality or major morbidity and no reoperation of donors	Similar studies included in table 2.
Shah SA, Grant DR, Greig PD et al. (2005) Analysis and outcomes of right lobe hepatectomy in 101 consecutive living donors. *American Journal of Transplantation* 5: 2764–9.	Prospective case series Canada (single centre) Donor 101 donors. RH-ALDLT (55 RH+MHV, 46 RH-MHV) FU: median 24 months. 2000–2004	Overall morbidity rate was 37%. All grade I or II, majority occurred during first 30 days. Removal of MHV did not affect morbidity rate. Fewer complications in the later half of experience. No mortality noted. All donors were well and returned to full activities.	Similar studies included in table 2.

Soejima Y, Taketomi A et al (2006). Feasibility of left lobe living donor liver transplantation between adults: an 8-year, single-center experience of 107 cases. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons.6: 1004-1011.	Retrospective case series 1996-2005 Japan n=107 left lobe, 50 right lobe. Follow-up: LL 1044 days RL 541 days	Post-operative liver function and hospital stay in LL donors were significantly better and shorter than that in RL donors, while the incidence of donor morbidity (16% vs 28%) was comparable between LL and RL donors. Total morbidity was 20% (20/157).	Similar studies included in table 2.
Soejima Y, Shirabe K et al (2012). Left lobe living donor liver transplantation in adults. American Journal of Transplantation.12: 1877-1885.	Retrospective comparative case series 1996-2007 Japan n=200 LL-LDLT vs 112 RL LDLT Follow-up: 10 years	The overall donor morbidity rates were comparable between LL and RL (36% vs 34.8%, NS), whereas postoperatively liver function tests and hospital stay were significantly better ($p<0.0001$) in LL donors.	Similar studies included in table 2.
Shin M, Song S, Kim JM e al (2012). Donor morbidity including biliary complications in living-donor liver transplantation: single-center analysis of 827 cases. Transplantation 93: 942-948.	Retrospective case series 1994-2005 South Korea (single centre) n=1000 (1162 LDL donors) LDLT A-A=893 A-P=107 2 retransplantation in donors	No donor mortality. 3.2% (37/1162) donors had major complications (grade III). Until 2001 The major complication rate was 6.7% with most occurring in right liver donors. Since 2002, donor complication rate reduced to 1.3%.	Similar studies included in table 2.
Sakamoto S, Nosaka S et al (2012). Living donor liver transplantation using grafts with hepatic cysts. Liver Transplantation. 18: 1415-1420.	Retrospective case series Japan 2005-2012 n=34 donors with hepatic cysts. LDLT Follow-up: median 3.1 years	All donors with cystic lesions were found to be doing well without any major postoperative complications. There were no significant differences in post-operative liver function with respect to type of surgery (TL, LL, or sectionectomy).	Donors with cystic lesions as liver donors.

Sultan, A. M., Salah, T., et al (2014). Biliary complications in living donor right hepatectomy are affected by the method of bile duct division. Liver Transplantation.20: 1393-1401.	Retrospective analysis n=216 donors with right hepatectomy (extrahepatic dissection group[EDG]- 108 vs fluoroscopy guided transection group[FGG]-108)	Intraoperative biliary complications did not differ between both groups, p = 0.313. The commonest postoperative complication was biliary leak/biloma accounting for 32.5% of all donor complications, followed by non-biliary fluid collections. 24 (11.1%) donors developed 27 biliary complications. The FGG showed significantly less biliary complications (5.6%, 6 donors), when compared to EDG (15.7%, 18 donors), p = 0.015. Grade 3 complications were significantly higher in EDG, p = 0.024. On multivariate analysis, the only significant factor predicting the occurrence of biliary complications was the use of fluoroscopy guided bile duct division, p = 0.009. In conclusion, we believe that the proposed method of biliary division is safe, simple and reproducible.	Larger studies included in table 2.
Taketomi A, Shirabe K.et al (2012). The long-term outcomes of patients with hepatocellular carcinoma after living donor liver transplantation: a comparison of right and left lobe grafts. Surgery Today. 42: 559-564	Retrospective review Japan 1995-2009 Donors (LL 82 versus RL 46) recipients with HCC Follow-up: mean 3.6 years RL, 3.5 years LL	The mean postoperative total bilirubin levels and duration of hospital stay after surgery of LL donors were significantly deceased compared to RL ($p<0.01$). The overall complications in RL was 13%, which was lower than LL group (23%), p=0.97. the rate of severe complications with LL was 6.2% and lower than RL (15.6%).	Reports primarily recipient outcomes.
Trotter JF, Adam R et al (2006). Documented deaths of hepatic lobe donors for living donor liver transplantation. Liver transplantation. 12:1485-1488.	Retrospective review	Deaths reported- I unknown cause (USA) at 3 days, 1 due to myocardial infarction at 4 days, I comatose and vegetative state at 2 days (India), 1 due to pancreatitis and sepsis at 30 days (USA)	Deaths already reported in study 1 in table 2.
Ueda M, Egawa H, Ogawa K et al. (2005) Portal vein complications in the long-term course after paediatric living donor liver transplantation. *Transplantation Proceedings* 37: 1138–40	Children 479 patients. FU: unclear. 1990–2003	8% of patients showed a portal vein complication.	Only looking at portal vein complications.
Usta S, Ates M et al (2013). Outcomes of left-lobe donor hepatectomy for living-donor liver transplantation: a single-center experience.	Retrospective case series 2006-12 USA (single centre) n=60	16 complications were seen in 20% (12/60) donors. Complications developed in 40% (6/15) LL donors, and in 13.3% (6/45) left lateral segmentectomy. 7 were grade	Similar studies included in table 2.

Transplantation Proceedings. 45: 961-965	LDLT –LL Follow-up: mean 30 months	1 and 2 were grade 2. Major complications consisted of 25% (4) grade 3a and 18.7% (3) grade 3b complications. No grade IV or V complications occurred.	
Umeshita K, Fujiwara K, Kiyosawa K et al. (2003) Operative morbidity of living liver donors in Japan. *Lancet* 362: 687–90.	Donor 1853 patients. FU: unclear. 1989–2002	Complications higher in donors of right lobes. No morality noted.	Survey of transplant centres in Japan – concerns about generalisability of results.
Verbesey JE, Simpson MA, Pomposelli JJ et al. (2005) Living donor adult liver transplantation: a longitudinal study of the donor's quality of life. American Journal of Transplantation 5: 2770–7.	Donor 47 patients. FU: 12 months. 2001–2004	Suggested that living live donors found the overall experience to be a positive one.	Similar studies captured in systematic review
Walter M, Papachristou C et al (2006). Impaired psychosocial outcome of donors after living donor liver transplantation: A qualitative case study. Clinical Transplantation.20: 410-415	Qualitative study Germany 2000-2002 n=6 donors with negative moods and physical complaints in psychometric monitoring 6 months after surgery.	6 donors reported various unspecific complaints and psychological conflicts. Sadness was expressed about organ rejection and death of recipient. Anxieties about the recipient and their won health were verbalised. Disappointment and anger refer to the experience that they were not fully appreciated by the medical system and social environment as expected. The negative emotions of donors with impaired psychosocial outcome could be related to a decrease in self-esteem in the postoperative course.	QOL
Wakade VA. and Mathur SK (2012). Donor safety in live-related liver transplantation. Indian Journal of Surgery 74: 118-126.	Donor safety review	Surgical mortality risk is estimated at 0.1% for left lobe donation and 0.5% for right lobe donation. Factors contributed to donor mortality and morbidity and strategies to reduce these are presented.	General review
Williams RS, Alisa AA, Karani JB et al. (2003) Adult-to-adult living donor liver transplant: UK experience [see comment]. *European Journal of Gastroenterology and Hepatology* 15: 7–14.	Adult 16 patients. FU: unclear. 1998–2002	Four patients died following sepsis.	UK experience – authors noted report details the first experience with this technique with patients from overseas.
Yang HR, Jeng LB et al (2012). Living donor right hepatectomy with inclusion of the middle hepatic vein:	Prospective case series Taiwan (single centre)	No donor admitted to intensive care after surgery. Post-operatively 19.5% (39/200) donors had grade I and II	Impact of RL-ALDLT with inclusion of middle hepatic

Outcome in 200 donors. Transplantation Proceedings.44: 460-462	2005-2011 n=200 donors RH with middle hepatic vein (MHV)-ALDLT Follow-up: not reported	complications, most minor wound infections or massive ascites needing diuretic therapy. 3.5% (7/200) had grade III complications, including 5 bile leakages requiring endoscopic biliary drainage and 2 abdominal wound dehiscence needing repair. No donor mortality.	vein (MHV) assessed.
Yilmaz S, Kayaalp C et al (2013). Single-center analysis of the first 304 living-donor liver transplantations in 3 years Hepato-Gastroenterology.60: 1105-1109	Prospective case series n=304 recipients (289 donors including 15 retransplants) Turkey 2007-2010 LDLT (95% RL) Follow-up: donors ranged from 1-3 years (median 26 months).	All 289 donors were alive and well after surgery. Overall postoperative complication rate was 26.4% (78 donors). Bile leakage (2%), intra-abdominal bleeding (2.3%), chylous peritonitis 0.6%, hepatic venous obstruction 0.3%, wound infection in 11.1%, incisional hernia 2.3%, and pulmonary complications 8.4%. reoperations needed in 5.4% (16 donors).	Similar studies included in table 2.
Yuan D, Wei YG, Li B et al (2011). Evaluation outcomes of donors in living donor liver transplantation: A single-center analysis of 132 donors. Hepatobiliary and Pancreatic Diseases International.10: 480-488	prospective case series n=132 donors China (single centre) 2005-2008 LDLT follow-up: 3 years	71.2% (94/132) donors developed postoperative complications. Grade I 34%, n=45, grade II 29.5%, n=39, Grade III 7.6%, n=10. There was no death or grade IV morbidity.	Similar studies included in table 2.
Yamamoto K, Takada, Y et al (2007). Nonalcoholic steatohepatitis in donors for living donor liver transplantation. Transplantation 83: 257-262.	Retrospective review Prevalence of non-alcoholic steatohepatitis (NASH) in LDLT donors and postoperative course for both donors and recipients of NASH grafts. 1998-2003 n=263 donors	NASH was diagnosed histopathologically in three cases (1.1%). Pathologic examination showed that a donor who died in 2003 had the most severe NASH among the three cases. The remaining two NASH donors had uneventful postoperative courses without complications. All grafts showed improvement with respect to the steatosis and histologic findings of NASH.	Death due to NASH already covered in table 2.
Yaprak, O., Dayangac, M et al (2011). Analysis of right lobe living-liver donor complications: A single center experience. Experimental and Clinical Transplantation.9: 56-59	Retrospective case series Turkey (single centre) 2004-2009 n=181 donors RL-ALDLT Follow-up: mean 33.3 months	40.3% (73/181) -81 complications occurred in donors. Most common was wound infection 7.7% (14/181). Biliary complications seen in 4.4% donors. No postoperative mortality, grade 4 complications did not occur. Blood transfusion need needed during surgery. Rate of reoperation was 1.6%.	RL-ALDLT Similar studies included in table 2.
Zeyneloglu P, Pirat A et al (2008). A comparison of right and left lobectomies for living donor liver	Retrospective review USA (single centre) 2003-2007	There was no significant differences in mean liver volume among the groups (p>.05). More patients in LLS	Impact on clinical outcome based on type of resection for

transplantation: an anesthesiologist's point of view. Transplantation Proceedings. 40: 53-56	LDLT donors 54 RL, 29 LL, 31 left lateral segment (LLS).	group required heterologous blood transfusion than those in other groups (p=.01). The incidence of intraoperative hypotension was similar for all groups (p>.05). RL group had a higher rate of intraoperative hypothermia than other groups (p=.01). There were no intraoperative respiratory complications or cardiac events.	LDLT.

Appendix B: Related NICE guidance for living-donor liver transplantation

Guidance	Recommendations
Interventional procedures	**Living-donor lung transplantation for end-stage lung disease. NICE interventional procedure guidance 170 (2006)** 1.1 Current evidence on the efficacy of living-donor lung transplantation for end-stage lung disease and its safety profile for suitable recipients appears adequate to support the use of this procedure. 1.2 The procedure should only be used in selected patients who would otherwise die. 1.3 However, limited evidence suggests that living-donor lung transplantation for end-stage lung disease carries a significant risk of morbidity for donors. Therefore clinicians wishing to undertake this procedure should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that donors receive thorough physical and psychological screening, and counselling about the morbidity associated with this procedure. They should also be provided with clear written information. In addition, use of the Institute's information for the public is recommended (available from www.nice.org.uk/IPG170publicinfo). • Audit and review clinical outcomes of all people donating lungs for transplantation. 1.4 Living-donor lung transplantation for end-stage lung disease should only be performed in specialist centres in the context of a multidisciplinary team. Donor lungs should be harvested by specialist thoracic surgeons. 1.5 Clinicians should enter all donors and recipients into the UK National Audit of Intrathoracic Transplantation (www.rcseng.ac.uk/research/ceu/projects/proj_intrathoracic.html).

Appendix C: Literature search for living-donor liver transplantation

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	11/03/2015	Issue 3 of 12, March 2015
HTA database (Cochrane Library)	11/03/2015	Issue 1 of 4, January 2015
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	11/03/2015	Issue 2 of 12, February 2015
MEDLINE (Ovid)	11/03/2015	1946 to March Week 1 2015
MEDLINE In-Process (Ovid)	11/03/2015	March 10, 2015
EMBASE (Ovid)	11/03/2015	1974 to 2015 Week 10
CINAHL (NLH Search 2.0)	11/03/2015	n/a
PubMed	11/03/2015	n/a
JournalTOCS	11/03/2015	n/a

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Living Donors/
2	((living or live) adj4 (donor* or donat*)).tw.
3	1 or 2
4	Liver Transplantation/
5	(Liver adj4 transplant*).tw.
6	4 or 5
7	3 and 6
8	((Live or auxiliary) adj4 liver* adj4 transplant*).tw.
9	(ALDLT or LDLT).tw.
10	7 or 8 or 9
11	Intraoperative Complications/
12	Postoperative Complications/
13	exp Safety/
14	exp Risk Factors/
15	exp morbidity/ or exp mortality/
16	((morbidit* or mortalit*) adj4 (event* or outcome*)).tw.
17	((intraoperative* or postoperative*) adj4 (complicat* or discomfort* or difficulty or difficulties)).tw.
18	safety.tw.
19	(side* adj4 effect*).tw.
20	(risk* adj4 factor*).tw.
21	(undesir* adj4 effect*).tw.
22	(treatment* adj4 emergent*).tw.
23	tolerability.tw.
24	(adverse adj4 (effect* or reaction* or event* or outcome*)).tw.
25	or/11-24
26	exp Liver Diseases/
27	(Liver* adj4 (disease* or failure* or cirrhosis* or cancer* or neoplasm* or cancer* or dysplas* or carcinoma* or adenocarcinom* or tumour* or tumor* or malignan*)).tw.
28	exp Hepatitis B/
29	exp Hepatitis C, Chronic/
30	Hepatiti*.tw.

31	(Hep adj4 (B or C)).tw.
32	exp Cholangitis, Sclerosing/
33	(Primary* adj4 scleros* adj4 cholangit*).tw.
34	(PSC or PBC).tw.
35	Biliary Atresia/
36	(Biliar* adj4 atresia*).tw.
37	or/26-36
38	10 and 25 and 37
39	Animals/ not Humans/
40	38 not 39
41	limit 40 to 20150331