Living donor liver transplantation: An overview

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No disclosures
Outline

• Current practice and limitations in liver transplantation
• Clinical overview of living donor liver transplantation
• Ethical considerations of living donor liver transplantation
Current state of liver transplantation

• Liver transplantation: safe and effective therapy
  • ~ 90% survival at 1 yr
  • ~ 75-80% survival at 5 yr

• Biggest limitation: organ shortage
  • 15K on waitlist, 20% mortality
  • Thousands of additional pts would benefit

• Use of “high-risk” deceased donor livers is common
  • Elderly (Age > 60)
  • Hepatic steatosis: fatty infiltration
  • Donation after circulatory death (DCD): warm ischemic injury
Current LT practices @ Duke: Phenotype of an aggressive center

Figure B10. Offer acceptance: Overall

Figure B14. Offer acceptance: Offer number > 50

Figure B13. Offer acceptance: HCV+ Donor

Figure B12. Offer acceptance: DCD Donor

July 2021
SRTR report
Current LT practices @ Duke: Phenotype of an aggressive center
Limitations of the current liver allocation system

- Aggressive utilization of deceased donor livers cannot fully overcome organ shortage
  - Waitlist mortality of 20%
  - Prolonged waiting time → patient deconditioning

- LT waitlist for deceased donors livers
  - Based on severity of illness: Model for End-Stage Liver Disease (MELD) score
  - Bilirubin, INR, creatinine
  - Median MELD at transplant @ Duke = 30

- “MELD purgatory”
  - Patients with decompensated liver disease, but lower MELD (15-30 range)
  - LDLT best addresses this population
Pros and Cons of LDLT

**Pros**
- Faster route to transplant
  - Limits disease progression (pts less sick)
  - Reduced waitlist morbidity/mortality
- Expansion of transplant indications
  - Advanced tumors
    - Hepatocellular carcinoma (HCC)
    - Intrahepatic cholangiocarcinoma
    - Colorectal liver metastases

**Cons**
- Potential for donor morbidity and mortality
- Greater technical complexity
  - Limited centers with necessary expertise
LDLT requires a careful balance between donor risk and recipient benefit
Outline

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• Clinical overview of living donor liver transplantation
• Ethical considerations in living donor liver transplantation
Historical perspectives

- LDLT first developed for pediatric recipients in the late 1980s
- Adult-to-adult LDLT developed in the 1990s
- LDLT has become commonplace in Asia due to low deceased donation rates (90% of transplants)
- LDLT acceptance has lagged in Europe and North America

americantransplantfoundation.org
Practice trends - USA

• In USA, LDLT in adults peaked in early 2000s, but declined over next decade
• Currently ~ 5% of transplants
• Most recent data suggests an increase in LDLT in USA

Trotter & Kam. Living Donor Transplantation: Evaluation and Selection in Adults, Transplantation of the Liver, Chapter 49, 659-666

Practice trends - worldwide

Rela et al. *Journal of Hepatology* 2021 vol. 75 975–980
Liver anatomy

By Polygon data is generated by Database Center for Life Science(DBCLS)[2] - Polygon data is from BodyParts3D[1], CC BY-SA 2.1 jp, https://commons.wikimedia.org/w/index.php?curid=45604146
Types of living donor grafts: Left lateral section graft

- Left lateral section graft (segments 2 & 3)
- Adult-to-pediatric donation
- Frequently parent → child
- Risk vs. benefit:
  - Low risk for donor: small portion of liver removed
  - Satisfactory graft size for infants/children

americantransplantfoundation.org
Types of living donor grafts: Right lobe graft

• Right lobe (segments 5,6,7,8) with or without the middle hepatic vein
• Usually adult-to-adult donation
• Risk vs. benefit:
  • 60-70% of liver removed from donor → potential morbidity
  • Large graft size → favorable for recipient

Types of living donor grafts: Left lobe graft

• Left lobe (segments 2, 3, 4)
• Adult-to-adult or adult-to-pediatric
• Risk vs. benefit:
  • 30-40% of liver removed from donor
    • Less morbidity than R lobe graft
  • Intermediate graft size → satisfactory for older children & small adults

Donor evaluation

- Donor safety is paramount in LDLT → evaluation must be comprehensive
- Living donors should be completely healthy: physically, mentally, and psychologically
- Medical history, physical examination
- Laboratory assessment: hematology, liver/renal biochemistry, coagulation, viral serologies
- Clinical psychological assessment
  - Motivation for donation, mental health history
- Social work assessment
  - Social support, relationship w recipient, behavioral health, substance use, finances
- Imaging assessment: CT scan + MRI/MRCP
  - Suitability of intended liver graft: anatomy, liver volume
Donor suitability

• No concerns from medical, surgical, psychological, and social work assessments
• Age eligibility: 18-60 (age range differs by center)
• BMI: < 30 preferred (cut-off differs by center)
• Anatomic considerations
  • Portal vein, hepatic artery, hepatic veins, and biliary anatomy must be suitable
  • Minimal hepatic steatosis
  • Volume of graft (and weight) is estimated by CT scan
  • Adequate graft size: Graft-to-recipient weight ratio (GRWR) > 0.8%
    • Example 1: 900 gram graft → 80 kg recipient: 1.1% (adequate size)
    • Example 2: 600 gram graft → 100 kg recipient: 0.6% (too small)
  • Adequate remnant liver volume in donor: > 30% of liver left behind
CT volumetry

Donor outcomes

• Long-term success of LDLT as a field depends on donor safety
• The goal for donor is a “textbook outcome”: safe procedure, no complications
• Impossible to achieve 0% morbidity and 0% mortality with major liver surgery
• What are acceptable rates of donor morbidity and mortality?
Right lobe living-donor hepatectomy—the Toronto approach, tips and tricks

Gonzalo Sapisochin\textsuperscript{1,2}, Nicolas Goldaracena\textsuperscript{1,2}, Jerome M. Laurence\textsuperscript{1,2}, Gary A. Levy\textsuperscript{1,3}, David R. Grant\textsuperscript{1,2}, Mark S. Cattral\textsuperscript{1,2}

- N = 469 right lobe donors from 2000-2014
- Median LOS: 6 days
- 0 periop donor deaths
- Overall complication rate: 12%
- Major complication rate: 2%
  - Anaphylaxis (N=1)
  - Pulmonary embolism (N=4)
  - Bile duct injury requiring reconstruction (N=2)
  - Narcotic overdose (N=2)
- Incisional hernias repaired in 5 pts > 1 yr post donation
Complications of Living Donor Hepatic Lobectomy—A Comprehensive Report

M. M. Abecassis\textsuperscript{a,*}, R. A. Fisher\textsuperscript{b}, K. M. Olthoff\textsuperscript{c}, C. E. Freise\textsuperscript{d}, D. R. Rodrigo\textsuperscript{e}, B. Samstein\textsuperscript{f}, I. Kam\textsuperscript{g}, R. M. Merion\textsuperscript{e,h} and the A2ALL Study Group\textsuperscript{i,†}

• US multicenter study: Adult-to-Adult Living Donor Liver Transplant (A2ALL)
• N = 740 living liver donors over 12 year period
• 40% of donors had some type of complication in 1\textsuperscript{st} year
• Overall rate of severe complications (grade 3 or 4): 1.1% (8 out of 740)
• Risk of complications increased with blood transfusions & intraop hypotension
• 3 donor deaths
  • 1 perioperative death due to sepsis/multi-organ failure
  • 2 late deaths following donation (drug overdose, suicide)
Trends and Health Care Outcomes Among Living Liver Donors: Are We Ready to Expand the Donor Pool With Living Liver Donations?

Sajid Jalil,1,2 Sylvester M. Black,3 Ken Washburn,3 Neil Rangwani,4 Alice Hinton,5 Sean G. Kelly,1,2 Lanla Conteh,1,2 James Hanje,1,2 Anthony Michaels,1,2 and Khalid Mumtaz1,2

- US national data from 2010-2017
- N = 1316 living liver donors
- 30 day and 90 day readmission rates of 5% and 5.9%
- Median LOS = 6 days
- Overall rate of complications: 42.8%
  - Male sex was independent predictor of complications (OR 1.63; 95% CI [1.19 – 2.23])
- 0 donor deaths during index admission or calendar year
Donor outcomes in anonymous live liver donation

Nicolas Goldaracena\(^1,2,\dagger\), Judy Jung\(^1,6,\ast,\dagger\), Aloysious D. Aravinthan\(^1,3,\dagger\), Susan E. Abbey\(^1,4\), Sandra Krause\(^1,4\), Cheryl Pritlove\(^1,5\), Joanna Lynch\(^1,4\), Linda Wright\(^1\), Nazia Selzner\(^1\), Jennifer Sturguris\(^6\), Paul Greig\(^1\), Anand Ghanekar\(^1,6\), Ian McIlvray\(^1\), Gonzalo Sapisochin\(^1\), Vicky Lee Ng\(^6\), Gary Levy\(^1\), Mark Catrall\(^1,6\), David Grant\(^1,6\)

* Toronto experience with 50 anonymous living liver donors from 2005-2017
  * Anonymous = no biological connection, no prior relationship
  * Also referred to as “non-directed” donors

* Most donors had a university education, middle-class income, and history of prior altruism
* Median age 38.5 yr

* 70% learned about liver donation via public (local, national) or social media
* 13 donors (26%) experienced a complication
  * 1 significant complication – re-operation for abdominal bleeding
* Median LOS 6 days
* Median time to return to work: 12 weeks
Transplant outcomes with LDLT
Recipient evaluation

• Standard multidisciplinary transplant evaluation
  • Hepatology, surgery, nutrition, social work, psychology, finance

• Specific considerations for LDLT
  • Recipient size (body weight)
  • Degree of portal HTN
  • Surgical issues
    • Extent of prior surgery (prior LT, liver resection)
    • Suitability of hepatic artery, portal vein (thrombus), vena cava
Retrospective review from University of Pittsburgh Medical Center, 2009-2019

- 245 LDLT vs. 592 DDLT
- LDLT demonstrated significantly better survival than DDLT (3 yr: 86% vs. 80%, p=0.03)
- LDLT had shorter LoS (11d vs. 13d, p=0.03)
- LDLT had lower rates of post-op dialysis (1.6% vs. 7.4%, p<0.01)
- Hospital costs 29.5% lower for LDLT
Meta-analysis and meta-regression of outcomes for adult living donor liver transplantation versus deceased donor liver transplantation

Arianna Barbeta¹,² | Mayada Aljehani³ | Michelle Kim¹,² | Christine Tien² | Aaron Ahearn¹,² | Hannah Schilperoort⁴ | Linda Sher¹,² | Juliet Emamuiel³

- Meta-analysis of 19 international studies comparing LDLT vs. DDLT, published from 2005-2017
- 4,571 LDLT vs. 66,826 DDLT
- LDLT associated with lower risk of patient death at 1, 3, and 5 yrs post-transplant
  - 1 year: 17% reduction in risk of mortality (HR 0.83 [0.76,0.90], p<0.0001)
  - 3 year: 15% reduction in risk of mortality (HR 0.85 [0.79,0.92], p<0.0001)
  - 5 year: 13% reduction in risk of mortality (HR 0.87 [0.81,0.93], p<0.0001)
- Graft survival similar between LDLT and DDLT
- LDLT had significantly lower MELD at transplant (p=0.04)
- LDLT had significantly shorter waiting time (mean difference 71 days, p<0.0001)
- Higher risk of biliary complications with LDLT (OR 2.14, p<0.0001)
Pts listed for transplant for hepatocellular carcinoma (HCC) at University of Toronto from 2000-2015

- N=219 with potential living donor (pLDLT) vs. N=632 with no living donor (pDDLT) @ time of listing
- Waitlist time (4.8 mos vs. 6.2 mos, p=0.02) and dropout rate (14.6% vs. 27.5%, p<0.001) were significantly lower in the pLDLT group
- Overall survival from time of listing significantly better in pLDLT group
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Ethical considerations

• Donor must explicitly express willingness to donate
• Donor must be free of coercion
• Informed consent
  • Review of planned operation (type of graft)
  • Estimated donor mortality of 0.5%
  • Estimated complication rate of 30%
  • Cumulative experience of the center and globally
  • Expected recipient outcomes: hospital mortality rate of 5% and 5 yr survival of 75-80%
30 living liver donors at Northwestern participated

Semi-structured interviews conducted after donor evaluation + informed consent

90% of LDs felt they had been informed “a great deal”

66% of LDs felt they understood information “a great deal”

40% reported difficulty comprehending medical terminology

Information LDs most desired:
  • Incidence/type of complications (67%)
  • Description of procedure (57%)
  • Process of donor preparation (43%)

Table 3. Risks identified by prospective liver donors.

<table>
<thead>
<tr>
<th>Risk</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>18 (60)</td>
</tr>
<tr>
<td>Bile leak</td>
<td>15 (50)</td>
</tr>
<tr>
<td>Infection</td>
<td>13 (43)</td>
</tr>
<tr>
<td>Liver failure</td>
<td>10 (33)</td>
</tr>
<tr>
<td>Bleeding</td>
<td>7 (23)</td>
</tr>
<tr>
<td>Anesthesia-related risks</td>
<td>6 (20)</td>
</tr>
<tr>
<td>Nerve-related risks</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Pain</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Depression and mental health risks</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Blood clots</td>
<td>2 (7)</td>
</tr>
</tbody>
</table>

What seems to be the riskiest aspect of donating? (n = 22)

<table>
<thead>
<tr>
<th>Risk</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>9 (41)</td>
</tr>
<tr>
<td>Surgery</td>
<td>4 (18)</td>
</tr>
<tr>
<td>Liver failure</td>
<td>3 (14)</td>
</tr>
<tr>
<td>Anesthesia</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Time lost at work</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Long-term risks</td>
<td>1 (5)</td>
</tr>
<tr>
<td>General complications</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Recovery</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Hernia</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Infection</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Pain</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Life-long need for medications</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Nothing</td>
<td>1 (5)</td>
</tr>
</tbody>
</table>

Percentages do not add up to 100% because participants could provide multiple responses.
What does the future hold for LDLT?

Pure laparoscopic living donor liver transplantation: Dreams come true

Kyung-Suk Suh | Suk Kyun Hong | Sola Lee | Su young Hong | Sanggyun Suh | Eui Soo Han | Seong-Mi Yang | YoungRok Choi | Nam-Joon Yi | Kwang-Woong Lee

Liver transplantation for non-resectable colorectal liver metastases: the International Hepato-Pancreato-Biliary Association consensus guidelines


Public Solicitation and The Canadian Media: Two Cases of Living Liver Donation, Two Different Stories

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