Role of Adult-to-adult Living Liver Transplantation in PSC

NORTHWESTERN
UNIVERSITY

Michael Abecassis, MD, MBA
J. Roscoe Miller Distinguished Professor
Departments of Surgery and Microbiology-Immunology
Chief, Division of Organ Transplantation
Dean, Clinical Affairs

PSC – Indications for Transplantation

- Cirrhosis with life-threatening complications
- Recurrent cholangitis with or without cirrhosis (intra or extrahepatic PSC)
- Stricture that is clinically significant and difficult to manage endoscopically
- Concern for cholangiocarcinoma

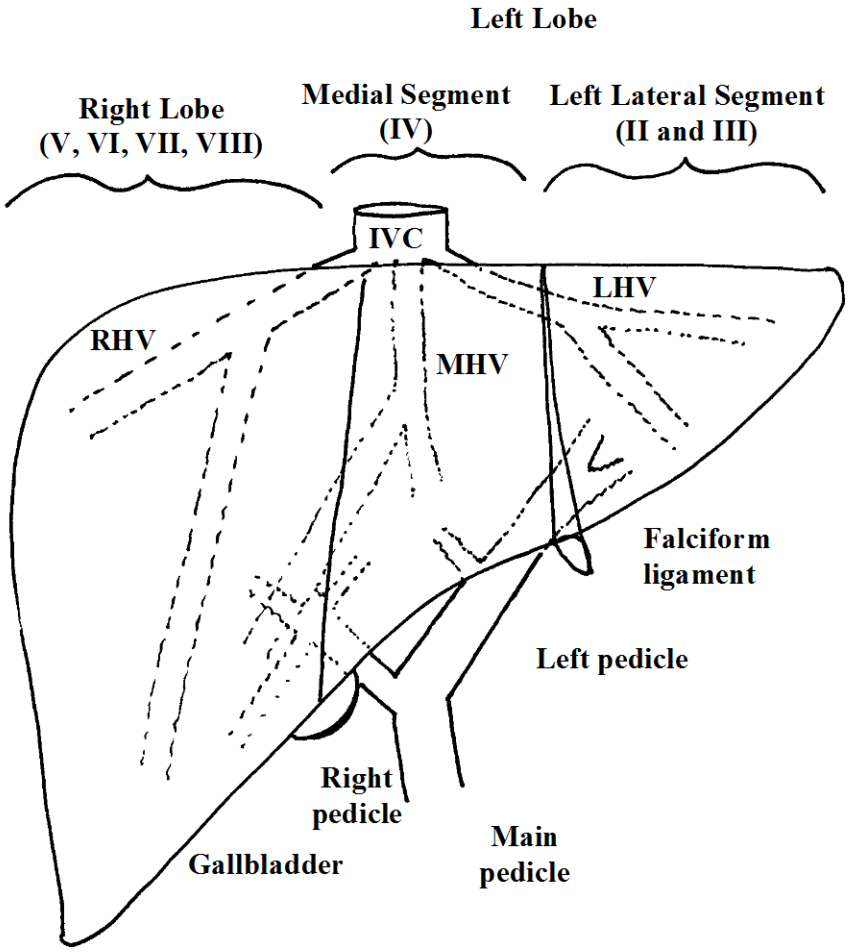
Cholangiocarcinoma

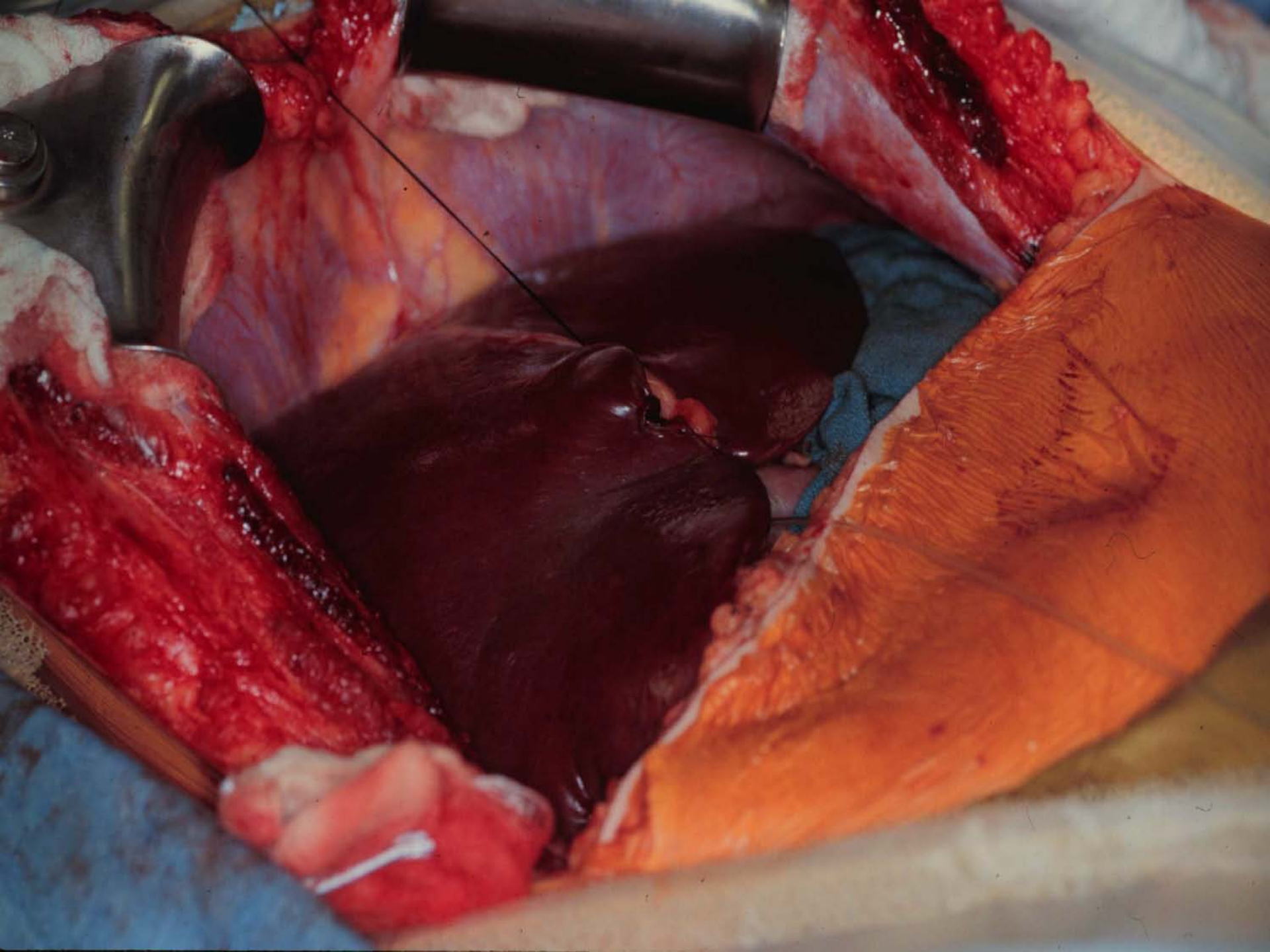
- 1% per year, 30% over 30 years
- Screening, difficulty in diagnosis
- No role for “prophylactic” transplantation
- If advanced, it becomes a contraindication to transplantation
- Requires pre-adjuvant treatment even in early stages

Problem

- MELD score is not helpful in cholestatic liver disease (T. Bilirubin not the driver)
- No significant MELD score upgrade for cholangiocarcinoma
- Difficult to diagnose early – no consistent biomarkers
- What to do if suspect cholangiocarcinoma but no other indications for transplantation

Surgical Anatomy of the Liver





Participating A2ALL Centers

University of Michigan

U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

ASTS
American Society of Transplant Surgeons

Columbia University Health Sciences

NORTHWESTERN UNIVERSITY

UCLA Healthcare

UCSF Medical Center

University of Colorado Hospital
University of Colorado Health Sciences Center
Denver, Colorado

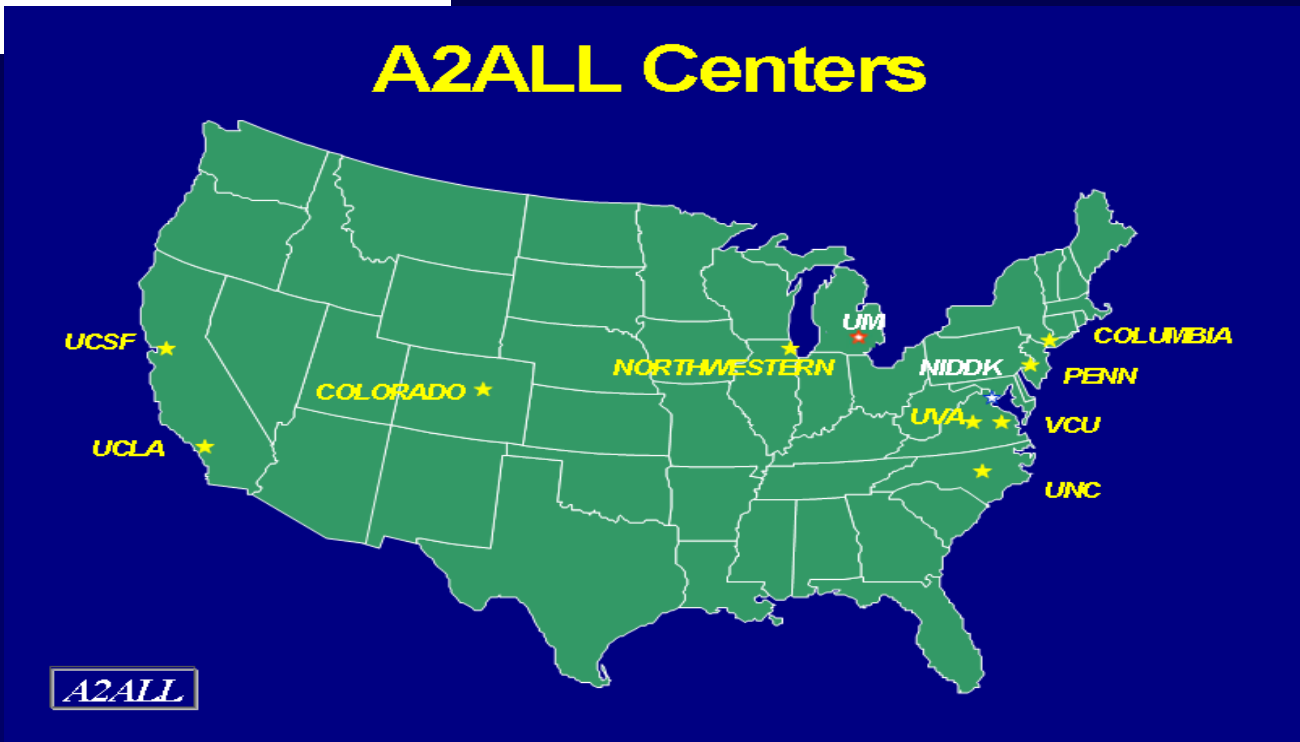
UNC HEALTH CARE

UNIVERSITY of VIRGINIA HEALTH SYSTEM

UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

VCU Health System
Virginia Commonwealth University

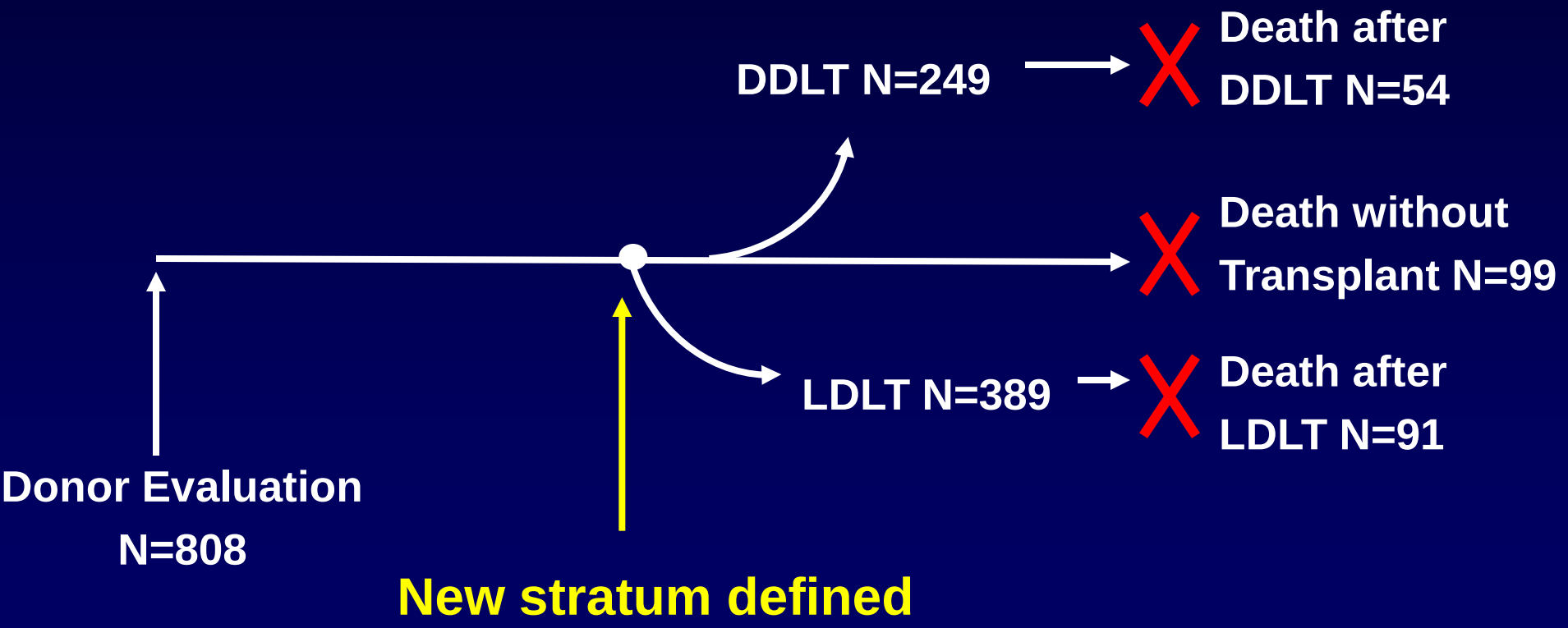
www.nih-a2all.org



A2ALL Prospective Cohort Study
Primary Aims

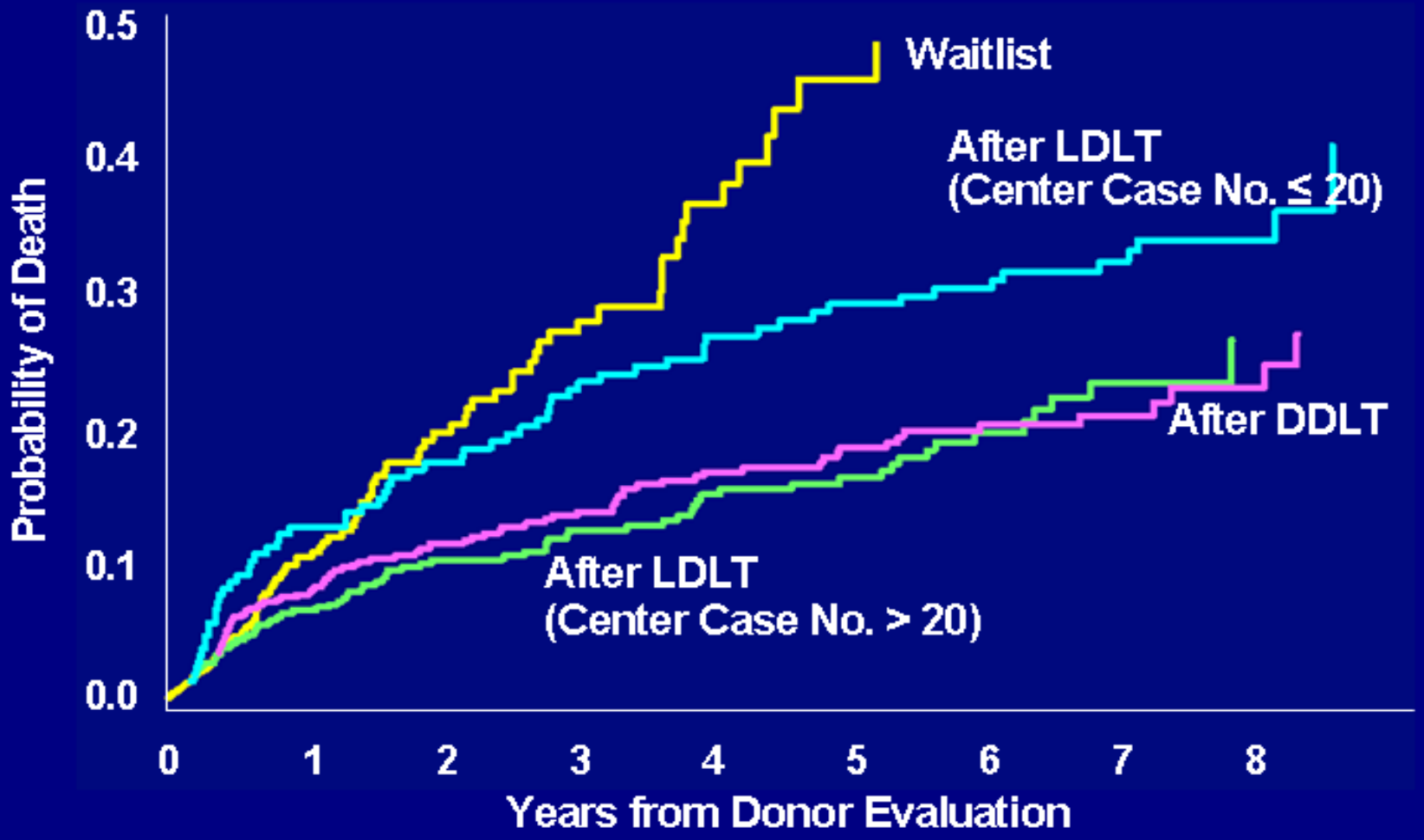
1. To characterize the differences between LDLT and DDLT in terms of post-transplant outcomes. To quantify the impact of choosing LDLT on the candidate for transplantation.
2. To assess LD outcomes (complications)
3. To determine short and long-term impact on QOL after donation compared to a control population
4. To standardize and assess the role of “informed consent” in affecting the decision to donate and satisfaction after donation

Analysis of Time from Evaluation of Potential Living Donor to Death: Sequential Stratification Approach



C. Berg et al, *Gastroenterology 2007*

Cumulative Risk of Death* after Initial Living Donor Evaluation by Transplant Group



A2ALL

* Estimates are adjusted for age, MELD score, and HCC status and apply to a patient with age 50 years, MELD 15, and no HCC.

[Updated from Berg Gatro.]

Conclusions

- Post-transplant survival after LDLT and DDLT in experienced centers is equivalent
- Adult LDLT is associated with lower candidate mortality compared with waiting for DDLT
  - Effect is magnified in experienced centers
- Lower mortality in LDLT recipients is associated with reduced exposure to wait list mortality
- Recipient complications decrease with experience

K. Olthoff et al. *Annals of Surgery* 2005
C. Berg et al. *Gastroenterology* 2007
C. Friese et al. *Am. J. Transplantation* 2008

A2ALL Prospective Cohort Study
Primary Aims

1. To characterize the differences between LDLT and DDLT in terms of post-transplant outcomes. To quantify the impact of choosing LDLT on the candidate for transplantation.
2. To assess LD outcomes (complications)
3. To determine short and long-term impact on QOL after donation compared to a control population
4. To standardize and assess the role of “informed consent” in affecting the decision to donate and satisfaction after donation

The Ultimate Sacrifice

A healthy man gives his brother half his liver—and dies. Should this kind of transplant be allowed?

By CHRISTINE GORMAN

MIKE AND ADAM HUREWITZ GREW UP together on Long Island, in the suburbs of New York City. They were very close, even for brothers. So when Adam's liver started failing, Mike offered to give him half of his. The operation saved Adam's life. But Mike, who went into the hospital in seemingly excellent health, developed a complication—perhaps a blood clot—and died last week. He was 57.

Mike Hurewitz's death has prompted a like bad odds, but there's more to this ethical dilemma than a simple ratio. The first and most sacred rule of medicine is to do no harm. "For a normal healthy person, a mortality rate of 1% is hard to justify," says Dr. John Fung, chief of transplantation at the University of Pittsburgh Medical Center. "If the rate stays at 1%, it's just not going to be accepted."

On the other hand, there's an acute shortage of traditional donor organs from people who have died in accidents or suffered fatal heart attacks. If family members fully understand the risks and are willing to

Complications After Living Liver Donation: A Prospective, Multi-center Report

Michael M. Abecassis, Kim M. Olthoff, James F. Trotter, Robert A. Fisher, Robert M. Merion, Lan Tong, Benjamin Samstein, Ronald W. Busuttil, Christopher E. Freise, Paul H. Hayashi, Carl L. Berg, and the A2ALL Study Group

Methods – Clavien Severity Grading System

Grade 1. Any alteration from ideal postoperative course with complete recovery, not requiring significant intervention

Grade 2. Requiring significant intervention or potentially life-threatening, but without residual disability or persistent disease

Grade 3. Any complication with residual or lasting functional disability or development of malignant disease

Grade 4. Complications that lead to transplantation or death

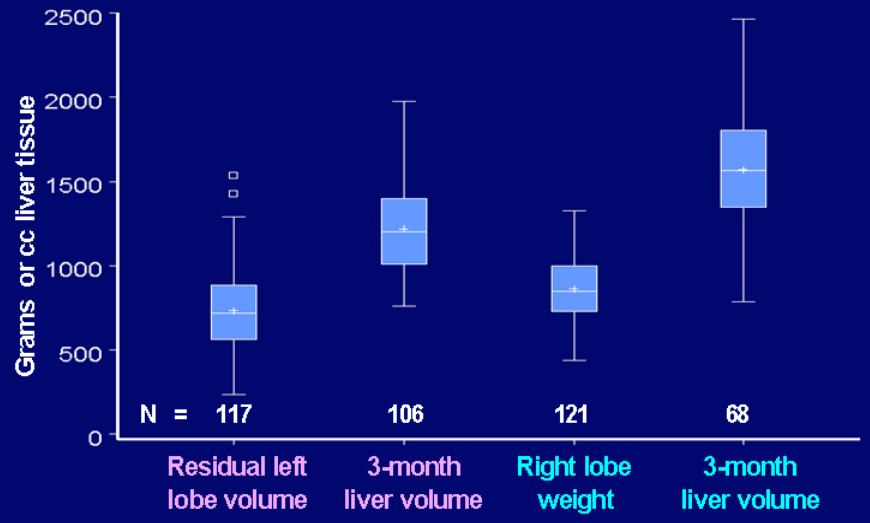
Summary

- 231 living liver donors with prospectively collected data using a standardized classification (up to 5-year follow-up)
- 3% incidence of aborted donations
- 29% of patients undergoing living liver donation had at least one complication
- Vast majority of biliary and infectious complications occurred within 30 days
- 4 Grade 3, 0 Grade 4 complications

Conclusions

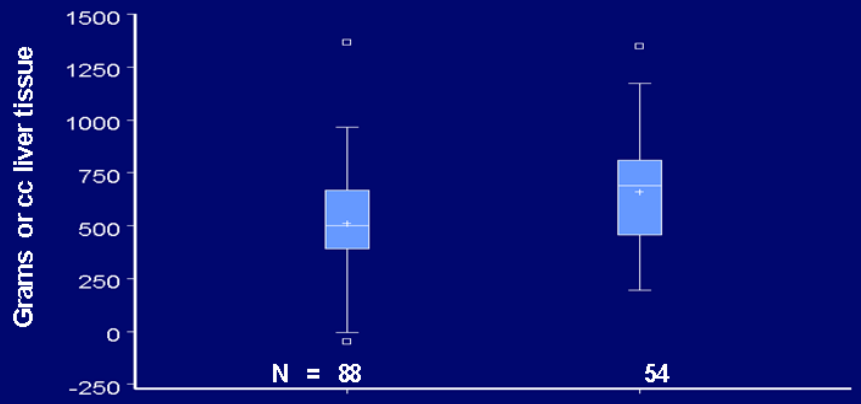
- These prospective data demonstrate that complications after living liver donation remain common and confirm our previous retrospective observations
- “Surgical complications” in this prospective cohort occurred significantly less frequently than in the retrospective cohort

Recipient and Donor Liver Volumes at Transplant and 3-Months



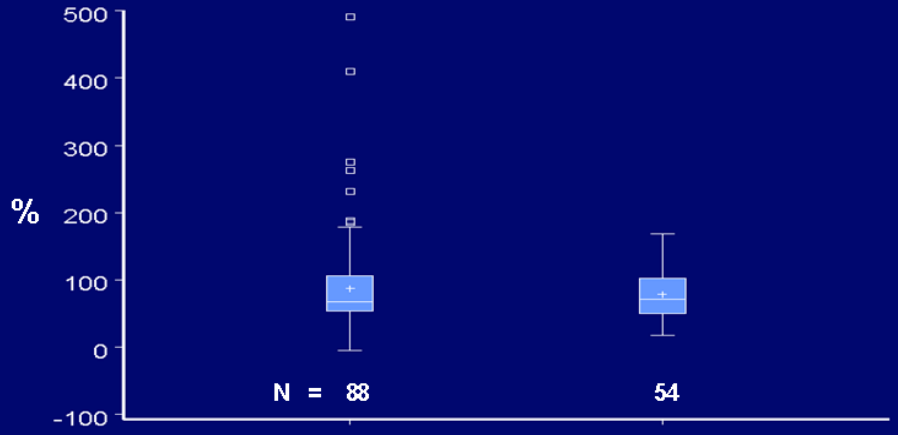
A2ALL

Absolute Increase in Liver Volume at 3 Months



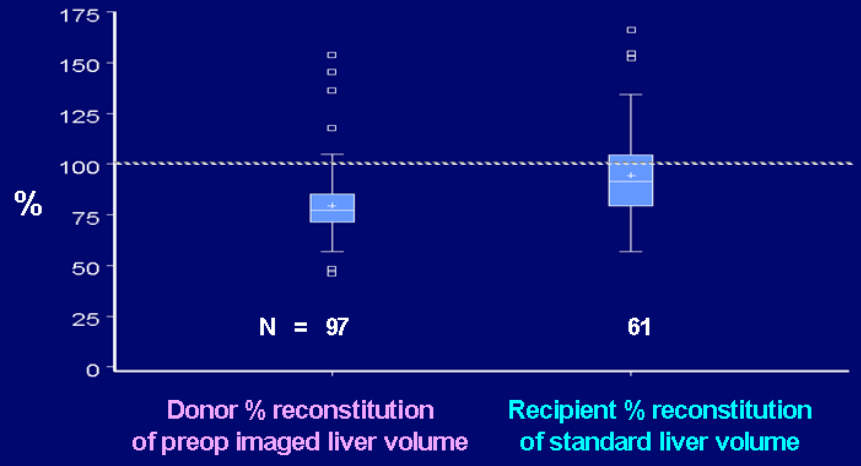
A2ALL

Percent Increase in Liver Volume at 3 Months



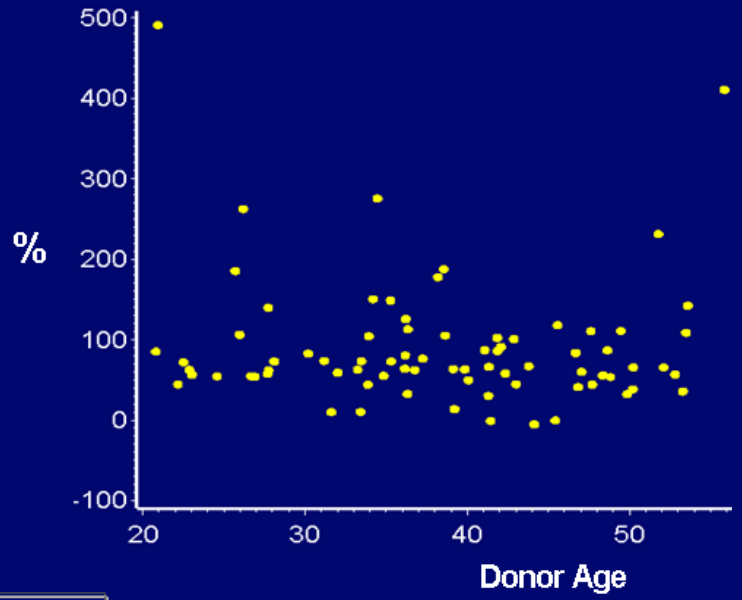
A2ALL

Percent Reconstitution of Liver Volume at 3 Months



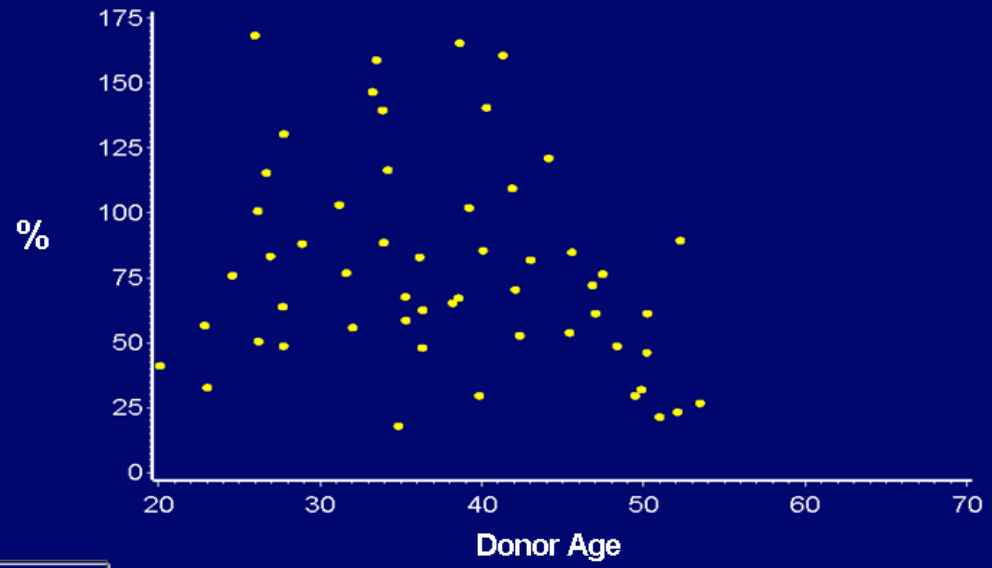
A2ALL

Donor Percent Increase in Size of Lobe by Donor Age



A2ALL

Recipient Percent Increase in Size of Lobe by Donor Age



A2ALL

A2ALL Participants

Center	Location	Principal Investigator
University of Michigan Health System-DCC	Ann Arbor, MI	Robert Merion, MD
University of Virginia	Charlottesville, VA	Carl Berg, MD
Columbia University	New York, NY	Jean Emond, MD
Northwestern University	Chicago, IL	Michael Abecassis, MD
University of Pennsylvania	Philadelphia, PA	Abraham Shaked, MD
University of Colorado	Denver, CO	James Trotter, MD
University of California	Los Angeles, CA	R. Mark Ghobrial, MD
University of California	San Francisco, CA	Christopher Freise, MD
University of North Carolina	Chapel Hill, NC	Jeff Fair, MD
Virginia Commonwealth University	Richmond, VA	Robert Fisher, MD
National Institute of Diabetes and Digestive and Kidney Diseases	Bethesda, MD	James E. Everhart, MD

A2ALL

Conclusions

- PSC has become one of the primary indications for LDLT
  - Low MELD score but need transplantation
  - Suspected cholangiocarcinoma
  - Cholangiocarcinoma
- LDLT is safe and effective once learning curve is conquered (15-20 cases)
- Prevalence and significance of donor complications seem to be improving