Liver Transplantation and ARPKD

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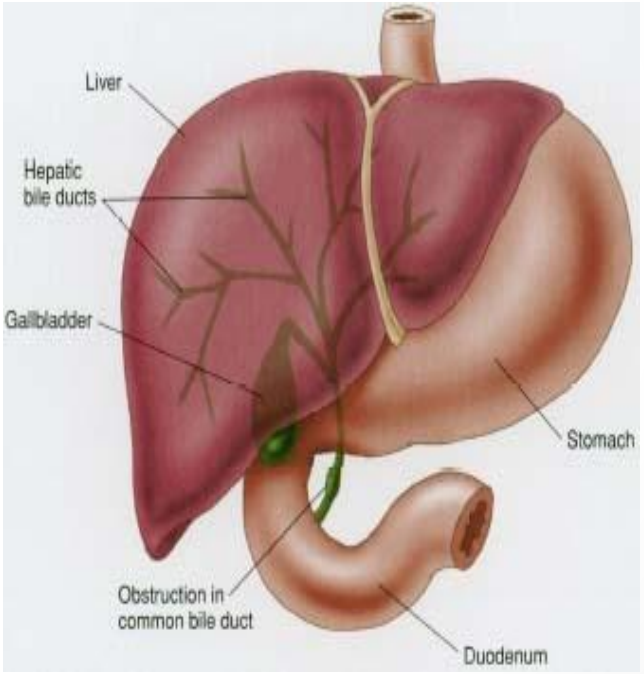
Objectives

- Primary functions of the liver
- Indications for Liver Transplant
- Process of liver transplant evaluation and listing
- Liver transplant surgery
- Unique challenges in ARPKD and liver transplant

Primary Functions of the Liver

- **The liver has several important jobs, of which the main ones include:**
  - Manufacturing bile
  - Making the proteins, including clotting factors
  - Metabolize sugar and protein, fat- converting the food we eat into chemicals necessary for growth
  - Detoxify
  - Maintain portal flow



Liver Transplantation - History

- 1963 - First liver transplants performed at 3 separate institutions, each resulting in death of the recipient
- 1967 - Successful transplants were done (the first in a child) but 1 year survival rates were dismal (30%).
- 1978 - The introduction of cyclosporine rapidly improved 1 year survival rates to up to 80% (for adults) and revolutionized the field of solid organ transplantation.

Liver Transplantation - History

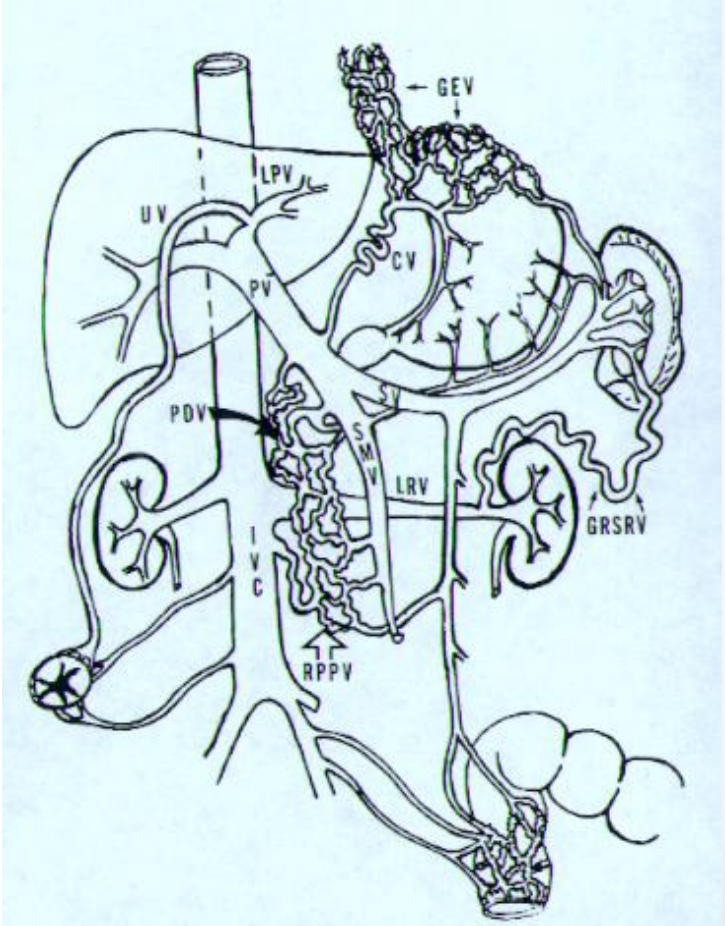
- 1980s - Numerous refinements of surgical techniques, organ procurement, preservation. Reduced size and split techniques introduced.
- 1989 - The first US living-donor (adult-to-child) liver transplantation was performed.
- 1993 - FDA approval of Tacrolimus (FK506) for primary immunosuppression.
- Current - Liver Transplantation is well established as useful therapy for children with end stage liver disease and for treatment of metabolic diseases correctable with hepatic replacement.

Common Indications for OLT in Pediatric Liver Disease

- Complications of cholestasis
  - Failure to thrive, pruritis
- Complications of synthetic failure
  - Coagulopathy, low albumin
- Complications of metabolic failure
  - Low blood sugar
- Complications of immune dysfunction
  - Biliary infections, peritonitis

Complications of portal hypertension

- Splenomegaly
- Ascites/peritonitis
- Varices
- Hepato-pulmonary syndrome
- Caput medusa
- hemorrhoids



Spleen guard

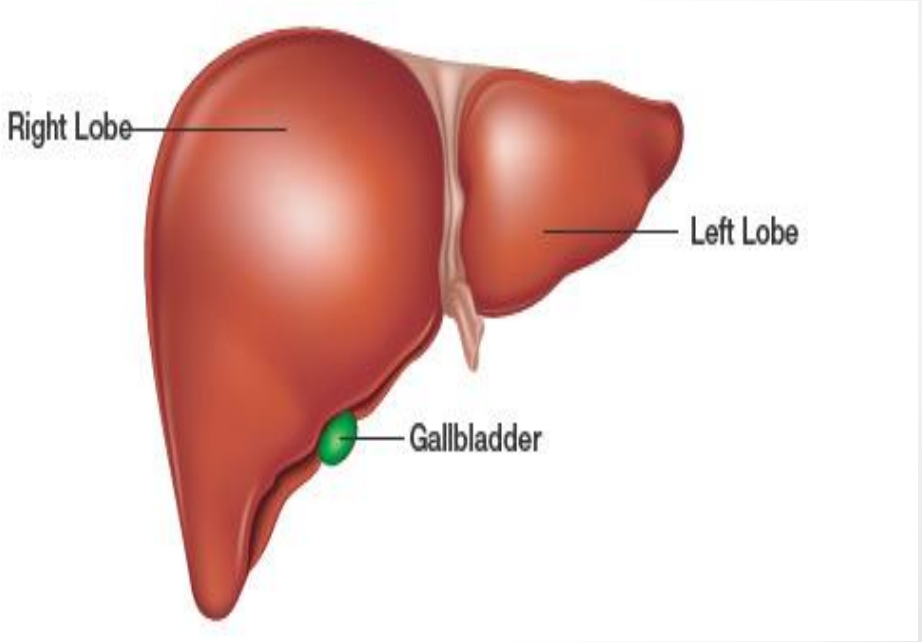
"Anything from the organ cart today, Mr.. Harrelson?"

Indications for OLT

- A chronic liver disease is not an *absolute* indication for transplantation
- A life threatening complication of liver disease is an indication for transplant (as are certain metabolic and malignant diseases)
- Given the seriousness of transplantation and the shortage of suitable donor organs, liver transplant should be avoided when possible
- Medical therapy for all complications of liver disease should be aggressively pursued to postpone or prevent need for liver transplantation.

Types of liver transplant

- Living Donor
  - Split/Segmented Liver
- Deceased Donor
  - Whole Liver
  - Split/Segmented Liver



Evaluation

- Consult to evaluate for transplant
- Family meeting
  - Educational materials provided to the family
- Patient undergoes extensive workup
  - Surgical Evaluation
  - Laboratory studies
  - Radiology imaging
    - Liver Doppler U/S
    - Neck vessels
    - ECHO
  - Anesthesia Consult
  - Psychosocial Consult
  - Transplant Pharmacist Consult
  - Nutrition Consult
  - Financial counseling

Evaluation of Children for Liver Transplantation

- Major goal of evaluation:
  - to determine if the child is likely to benefit from OLT
- Additional goals:
  - consider alternative management
  - predict optimal timing
  - maximize nutritional/medical Rx
  - provide education to patient and family

Listing

- Patient data entered into UNOS (United Network of Organ Sharing) online secure system
- Assigned a "score"
  - End-stage liver disease score (MELD/PELD)
  - Calculation based on lab values and growth measures
  - Higher score indicates more urgent need for transplant
  - Exception points - Given via review board for patients with severity of disease not reflected by lab values

Waiting….

Organ Allocation

- Livers are matched by
  - Size
  - Blood Type
  - HLA typing is not necessary for liver transplant
- Allocation is based on severity of illness, or "sickest first"

Pediatric Liver Transplant

In 2018

- New waitlist registrant 11,844
- Adult liver transplant 8250
- Pediatric liver transplant 563
- 5 year graft survival: 81.5%
- 5 year patient survival: 88.4%
- UNOS: www.unos.org
- SRTR: www.ustransplant.org

Unique considerations in ARPKD

- Kidney and liver transplantation is sometimes needed
- Question regarding timing and sequence of transplants
- Question about prognosis/outcome after tranplant

APRKD and Transplants

- Retrospective cohort study of all pediatric kidney and liver transplants performed in the U.S. from 1990 to 2011 for fibrocystic liver disease
- Data Source: Scientific Registry of Transplant Recipients (SRTR)
  - National database of all donors, wait-listed candidates and transplant recipients in the U.S.
- Age $\leq$ 18 years at initial liver or kidney transplant
  - Kidney transplant recipients with diagnosis code: polycystic kidney disease, nephronophthisis
  - Liver transplant recipients with diagnosis code: congenital hepatic fibrosis, Caroli's disease

Result

Initial organ transplant	Number of patients	Age at initial transplant (IQR)	Death (%)
Liver	73	8.7 (2.3, 13.3)	17 (23%)
Kidney	602	9.9 (3.5, 14.8)	59 (10%)
Simultaneous liver/kidney	41	9.2 (5.3, 13.8)	5 (12%)
Total	716	9.7 (3.6, 14.7)	81 (11%)

- Median follow up 8.5 years (IQR 4.7, 13.3)

Subsequent transplantation in organ transplant recipients

Initial organ transplant	Re-transplant	Re-transplant with SLK	Mean duration (yrs)*	Median age (yrs)
Liver	14 (19%)	0 (0%)	0.2 (0.01, 3.6)	11.8 (5.2, 14.2)
Kidney	116 (19%)	14 (2%)	7.7 (3.3, 10.5)	17.6 (11.3, 22.1)

2 of the 41 SLK (5%) were re-transplanted. 1 liver then kidney, 1 SLK.

*Interquartile range in parenthesis
SLK- simultaneous liver kidney transplant

Subsequent transplantation in alternate organ

Initial organ transplant	Transplant in alternate organ	Mean duration (yrs)*	Median age (yrs)
Liver	4 (5%)	8 (6, 10.4)	14.5 (10.9, 19.5)
Kidney	15 (2%)	4.6 (3.4, 8.6)	9.5 (7.2, 16.7)

Conclusions

- Patients with fibrocystic liver disease are much more likely to receive kidney transplants then liver transplants
- Risk of needing transplantation in an alternate organ is low in both liver and kidney transplant recipients, suggesting patients with end-stage disease of one organ are unlikely to develop end-stage disease in the other organ.
- Of the patients who underwent SLK, the mortality rate at end of follow up period is comparable to single organ transplants

Chris Klug

Liver transplant recipient 2000
Olympic bronze medalist 2002

Summary

- Liver Transplantation is a successful treatment for serious liver disease
- Outcome is very good and normal quality of life is the goal
- Special consideration in PKD/CHF should be given to status of kidney disease and possible need for liver and kidney transplant