AT THE FOREFRONT UChicago Medicine

Multiple-Organ Heart Transplantation

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Section Chief, Cardiac Surgery

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Disclosures

- None

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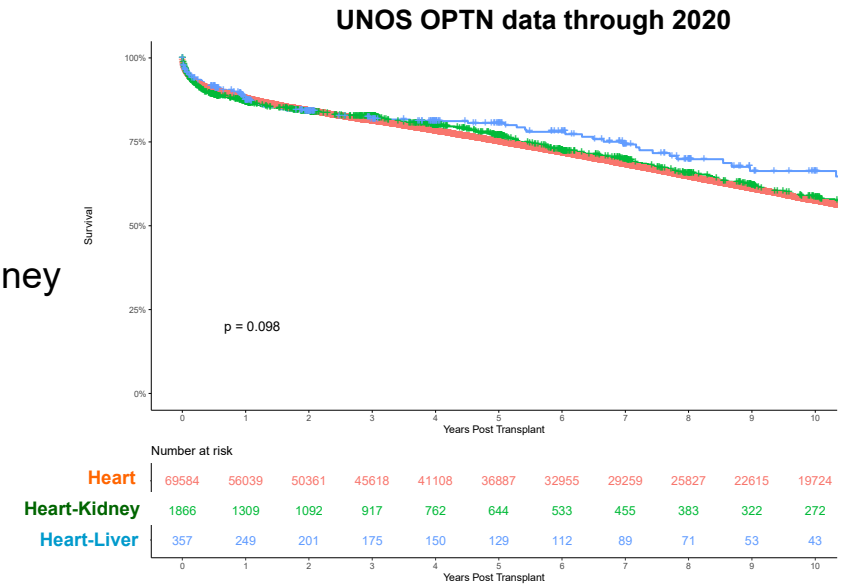
Outline

- Heart transplant
- Heart - Kidney
- Heart - Liver
- Heart - Liver – Kidney
- UCMC Program

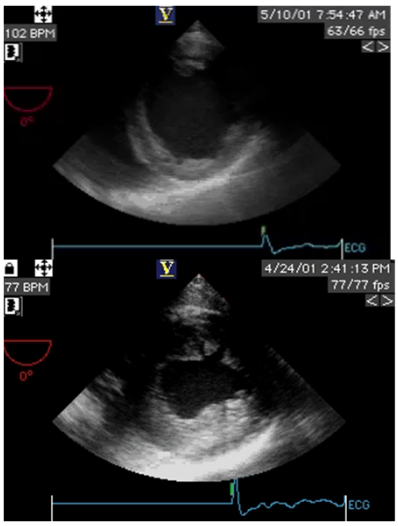


Heart Transplantation

Cardiac transplantation: recipient criteria (general)

End stage heart disease with <50% 1 year survival

- ischemic
- dilated / idiopathic
- valvular
- Congenital



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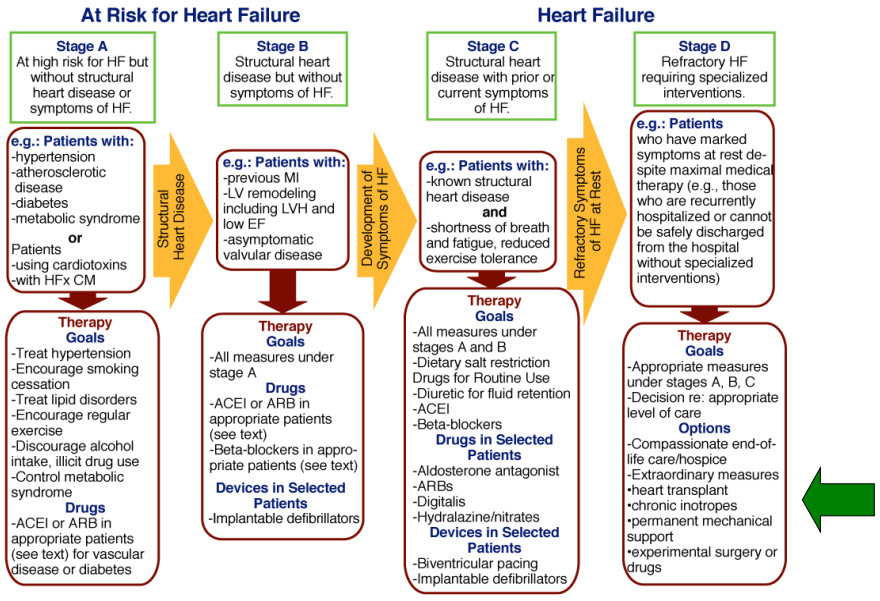

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Cardiac transplantation: recipient criteria (general)

- Maximum oxygen consumption VO_2<12 cc/kg/min
- Malignant intractable arrhythmias
- Inoperable ischemia
- Debilitated life style

Cardiac transplantation: recipient criteria (specific)

- Age: 0-70 years, program specific
- Reversible pulmonary hypertension with PVR<6 woods units
- Malignancy: disease free for 5 years
- No active infection (HIV??)
- No pulmonary infarction or CVA within 6 weeks
- No active alcohol or drug abuse
- Not obese (BMI<36)
- No irreversible end organ damage from diabetes
- *No significant liver/renal/pulmonary disease which could decrease lifespan*
- Compliance
- Insurance

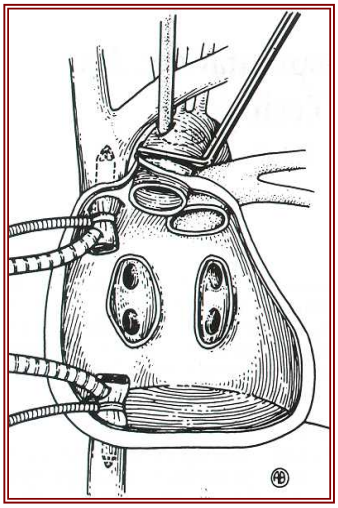
Listing procedure

- UNOS Heart Allocation *(Oct 2018)*
  - 1: VA ECMO; BiVAD non-dischargeable non-endovascular; LVAD life threatening arrhythmias
  - 2: TAH; BiVAD; RVAD; VAD for single ventricle; LVAD non-dischargeable non-endovascular' LVAD malfunctioning; Endovascular assist device (IABP, Impella); VT/VF
  - 3: LVAD 30 day time; inotropes plus monitoring; LVAD with hemolysis/pump thrombosis/RHF/device infection/bleeding/AI; VA ECMO/IABP/Impella after 14 days
  - 4: LVAD; inotropes no monitoring; congenital; intractable angina; re-transplant; restrictive
  - 5: Multiple organ
  - 6: Listed stable
- Multiple organs – organ with highest priority pulls other organs
  - Within 500 miles mandatory share
- PRA > 15%, crossmatch
- Weight range
  - low: 30-50%, depends on PVR
  - high: up to 999, depends on size of pericardial space
- Blood type compatible

Heart procurement: timing

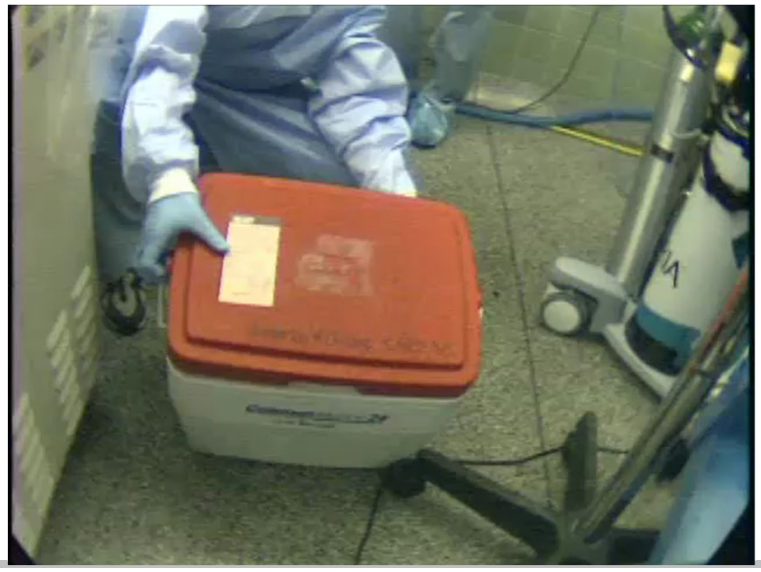
- Arrival 30 minutes before liver complete; may need more time if heart is to be resuscitated
- Ischemic time $\leq$ 4 hours
- Donor organ arrives at time of recipient cardiectomy
  - cardiectomy takes 45 minutes in primary operation
  - 1.5 to 2 hours in reoperation – longer with LVADs

OHT (total) - Explantation

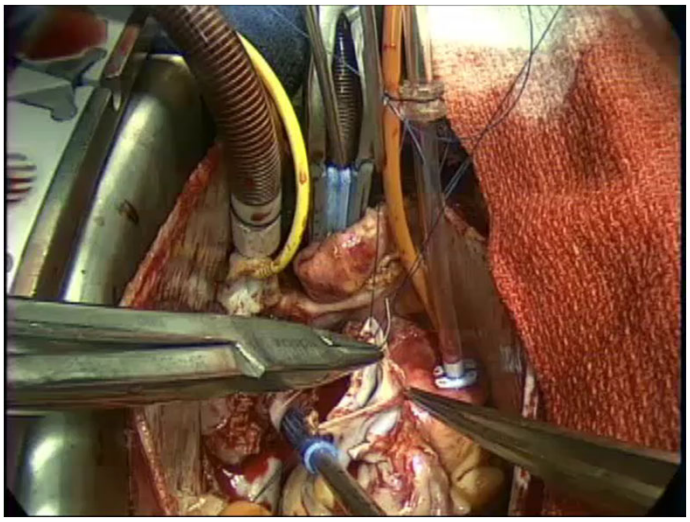


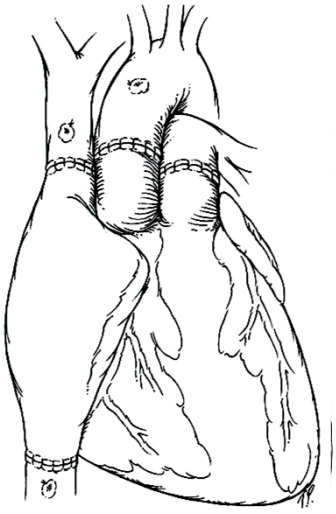
Total technique

OHT-Donor Preparation



OHT- Implantation



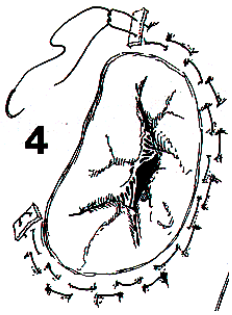


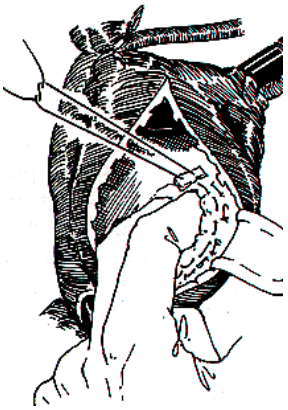
Tricuspid annuloplasty

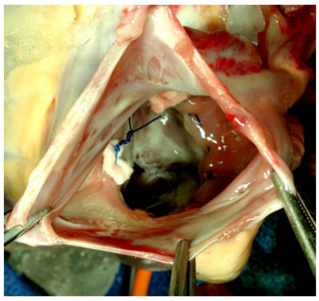
- Right heart dysfunction primary effect of rejection and/or preservation injury
- Leads to tricuspid regurgitation
  - renal dysfunction
  - long term residual effect with decreased survival
- TR treated with annuloplasty or replacement
- Randomized study of prophylactic tricuspid annuloplasty –

Jeevanandam V, Russell H, Mather P, Furukawa S, Anderson A, Raman J. 2006. Donor tricuspid annuloplasty during orthotopic heart transplantation: long-term results of a prospective controlled study. The Annals of Thoracic Surgery 82(6):2089-95

DeVega tricuspid annuloplasty







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Results - summary

- Improves RV performance : Perioperative period (0-7days)
  - Shorter reperfusion time
  - Lower CVP, higher mPA-CVP difference
  - Lower mortality
  - Less TR overall and less % with >moderate TR
- 5 years
  - Less TR
  - Less progression in TR
  - Fewer pts with >moderate TR
  - Improved renal function
    - Lower creatinine
    - Smaller increase in creatinine from baseline values
- Helps survive major hemodynamically compromising rejection
- **UCMC** – significant TR 2.9% vs reported 20-40%

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Sternal issues

- Risk factor for dehiscence or mediastinitis
  - Obesity
  - Multiple sternotomies
  - Peri-transplant low cardiac output with high dose inotropes
  - Bleeding
  - Immunosuppression
- Incidence 15%

Technique

-VS-

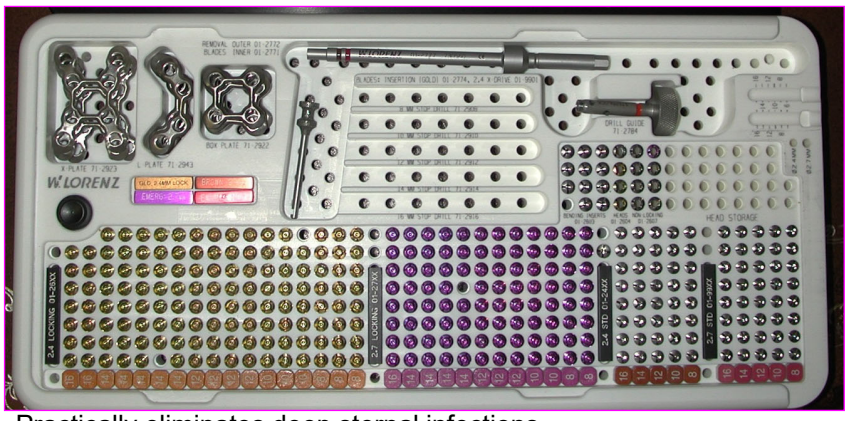
Results - Song DH, Agarwal JP, Jeevanandam V. 2003. Rigid sternal fixation in the cardiac transplant population. The Journal of Thoracic and Cardiovascular Surgery 126(3):896-7.

Retrospective Comparison (July 2000-July. 2004):

Total OHT Procedures	n= 120
Total high risk OHT	n= 72

High Risk Patients	Post-op sternal issues
Wire Closure n= 42	7 (16.7%)
Plate Closure n= 30	0

Titanium Sternal Fixation Screws



Practically eliminates deep sternal infections
Decreases pain
Decreases rehab/restriction periods
Decreases bleeding

Increasing Existing Donor Pool

Transmedics OCS

- **EXPAND Trial**
  - **Results of heart donors considered high risk**
  - **FDA approval**
  - **Evaluate with lactate and coronary flow**
  - **Visualization**

Results of OHT

- Standard immunosuppression
  - Tacromilus/ CellCept / steroids
- Excellent results
  - Survival
    - **1 yr: 85-90%** **10yr: 65%**
    - **5 yr: 70-75%**
- 90% return to work
- 95% NYHA class 1 or 2
- Complications due to immunological barrier

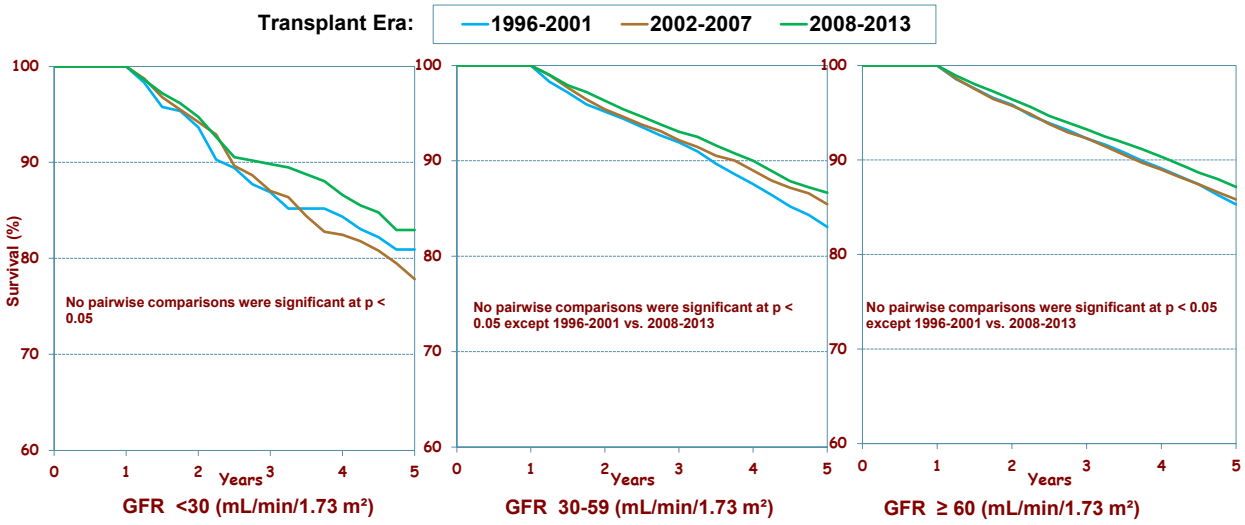
Heart – Kidney Transplant

Heart-Kidney Transplant

•Why?

- GFR decreases after HT due to calcineurin inhibitors, rapamycin, anti-virals
- Lower recipient GFR decreases HT survival

Adult Heart Transplants Kaplan-Meier Survival within 5 Years Conditional on Survival to 1 Year by Recipient GFR* and Era (Transplants: Jan 1996 - Jun 2013)



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Note: Y-axis is truncated for clearer presentation

* GFR was estimated using the Cockcroft-Gault formula

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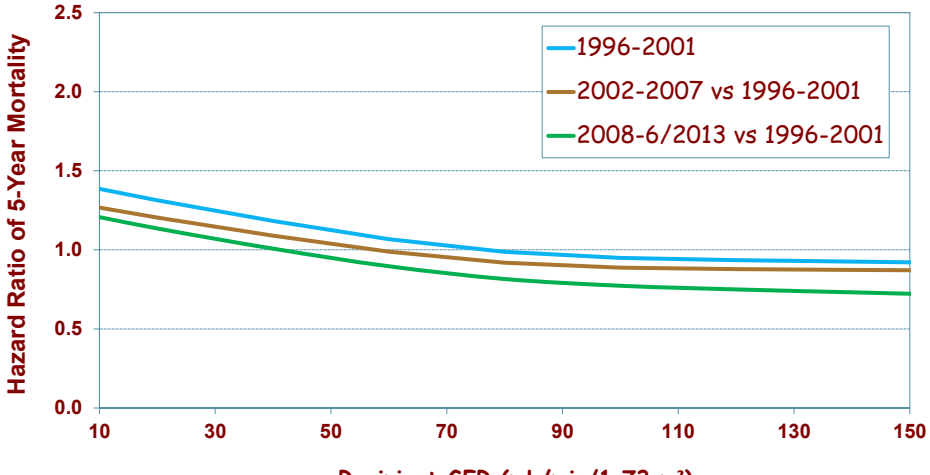
Adult Heart Transplants (1996-6/2013)
Risk Factors For 5-Year Mortality Conditional on Survival to 1 Year

Transplant era and recipient GFR* interaction



(N = 53,105)

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*Estimated using the Cockcroft-Gault formula

p-value for era < 0.0001; p-value for GFR < 0.0001; p-value for interaction = 0.6226

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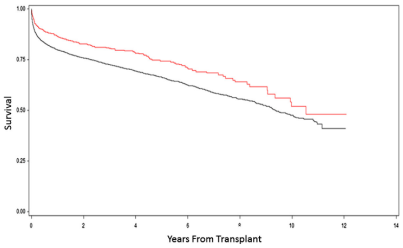
Heart-Kidney Transplant

- Why?
  - GFR decreases after HT due to calcineurin inhibitors, rapamycin, anti-virals
  - Lower recipient GFR decreases Heart alone survival
  - Combined Heart-Kidney decreases mortality in pts with GFR<37



Combined heart-kidney transplant improves post-transplant survival compared with isolated heart transplant in recipients with reduced glomerular filtration rate: Analysis of 593 combined heart-kidney transplants from the United Network Organ Sharing Database

Tara Karamlou, MD,[a] Karl F. Welke, MD,[b] D. Michael McMullan, MD,[b] Gordon A. Cohen, MD,[c] Jill Gelow, MD,[c] Frederick A. Tibayan, MD,[d] James M. Mudd, MD,[e] Matthew S. Slater, MD,[f] and Howard K. Song, MD[g]

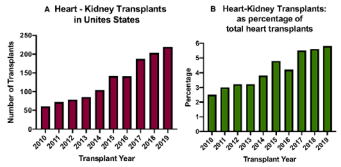
  - Consensus document 2020
    - <37 HKT appropriate
    - 37-50 prove organic disease
    - >50 HT alone

Consensus conference on heart-kidney transplantation

Am J Transplant. 2021;21:2459–2467.
Jon Kobashigawa[1] | Darshana M. Dadhania[2] | Maryjane Farr[3] | W. H. Wilson Tang[4] | Arvind Bhimaraj[5] | Lawrence Czer[1] | Shelley Hall[6] | Abdolreza Haririan[7] | Richard N. Formica[8] | Jignesh Patel[1] | Rafael Skorka[1] | Savitri Fedson[9] | Titte Srinivas[10] | Jeffrey Testani[8] | Julie M. Yabu[11] | Xingxing S. Cheng[12] | on behalf of the Consensus Conference Participants

Heart-Kidney Transplant

- Volume
  - Increasing



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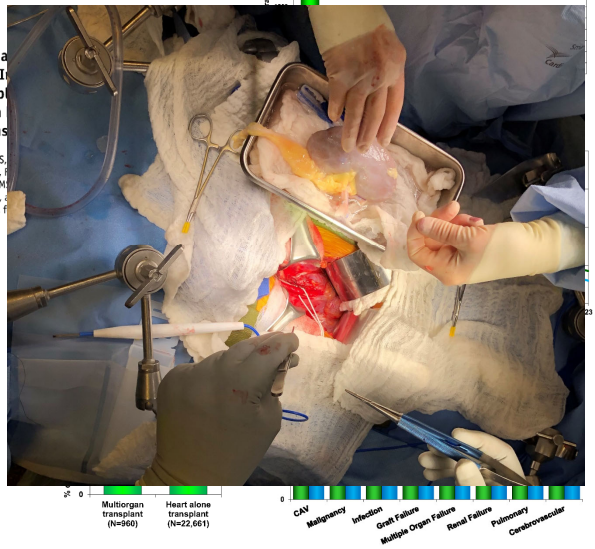
- Differentiate Cardiorenal vs Intrinsic Irreversible disease
- Workup
  - GFR
  - Imaging – ultrasound
  - Biopsy

Heart-Kidney Transplant

- Usually heart pulls the kidneys
- Ethical concerns
  - Removing kidney from pool
  - One patient instead of two
- Living donors
- Proposed safety net
  - GFR <20 within 365 days of HT (proposed)
- Actual Procedure:
  - Avoid femoral lines on side of kidney
  - Immediate vs pumping kidney and placing when recipient more stable
  - Wound issues
- Outcomes
  - Survival
  - Rejection
  - Complications

The Internationa
Registry of the I
and Lung Transpl
Transplantation
Multiorgan Trans

Kiran K. Khush, MD, MAS,
Daniel C. Chambers, MD,
Anna Y. Kucheryavaya, M
Joseph W. Rossano, MD,
Josef Stehlik, MD, MPH,
Transplantation



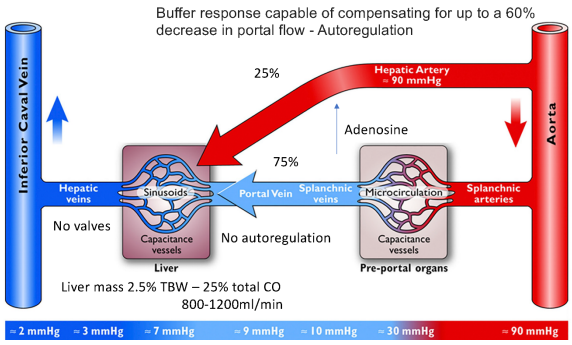
Heart – Liver Transplant

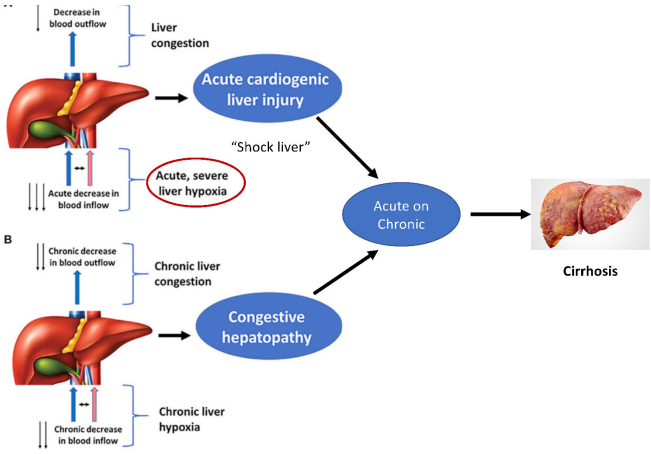
Heart-Liver Transplant

- Why?
  - HT or any Cardiac Surgery in patients with cirrhosis bad idea – 50% mortality
    - MELD score >13 generally considered contraindication to cardiac surgery
    - Complications: bleeding, vasoplegia, infection, primary graft dysfunction
  - LT with cardiac dysfunction bad idea – huge stress on heart, especially RV
    - LT with intra-transplant ECMO support possible
- Indications
  - Infiltrative – Amyloid
  - Congestive hepatopathy

Congenital – failed Fontan	Tricuspid Regurgitation/stenosis	LV Failure
Constrictive pericarditis	RV failure	Cardiac tumor

Pathophysiology of Cardiac – Liver Injury



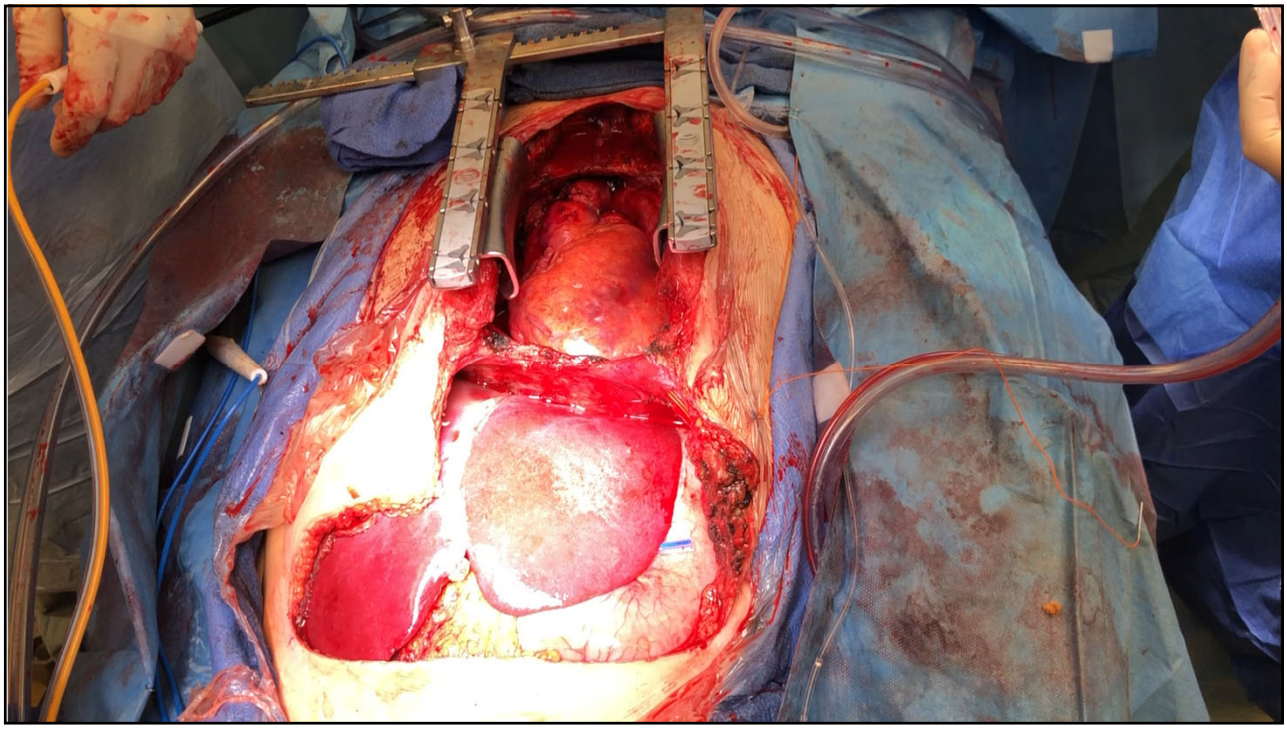


Heart-Liver Transplant – surgical technique

- HT followed by delayed different donor LT – bad idea, loss between transplants
- HLT same donor, liver first
  - Indications: high PRA
  - Issues: 1) Need to support heart during LT 2) Prolonged HT ischemic time
  - Significantly higher risk for mortality – aHR 2.44
- HLT same donor, simultaneous
  - Indications: decrease liver ischemic time, eliminate IVC anastomosis, decrease antibody exposure
  - Cumbersome, especially for complex reoperations
  - Mortality aHR 1.39
- HLT same donor, heart first (UCMC preference)
  - Coordination between HT and LT teams to minimize ischemic times
    - Heart dissection must be finished by the time organ arrives
    - Liver back table preparation at time of final heart anastomosis

Heart-Liver Transplant – surgical technique

- HLT same donor, heart first (UCMC preference)
  - HT must be hemostatic and without complications
  - Normal inotropes
  - Completely reverse heparin – ready to close
  - Place on ECMO (CentraMag) via femoral vein, SVC and aorta
  - 3 L/Min, maintain inotropes
  - Liver team proceeds without anti-coagulation for ECMO
  - Increase ECMO flow during times of hemodynamic instability
  - After LT, wean off ECMO
  - De-cannulate, close with plates
  - Liver team closes
- Immunosuppression: tacrolimus, CellCept, Steroids
- Complications: 1)bleeding 2) Liver perfusion 3) Bile ducts 4) Intra-abdominal abscess 5) Wound healing



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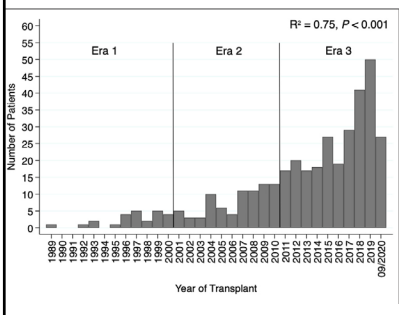
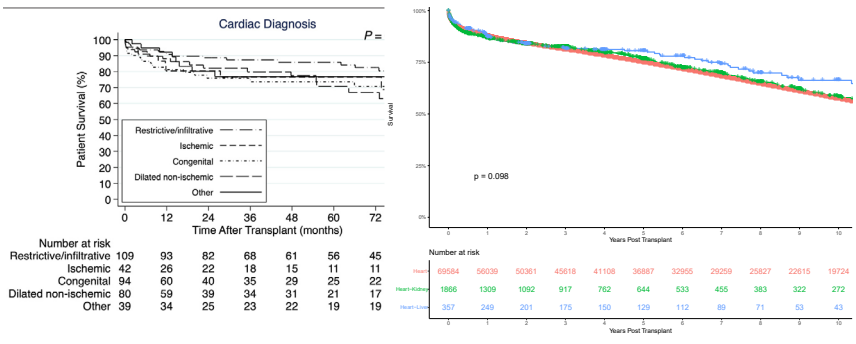
Heart-Liver Transplant – Summary of US experience

- Alexopoulos, et al. Transplant International. 2022,V35, article 10036
  - Volume HK and results





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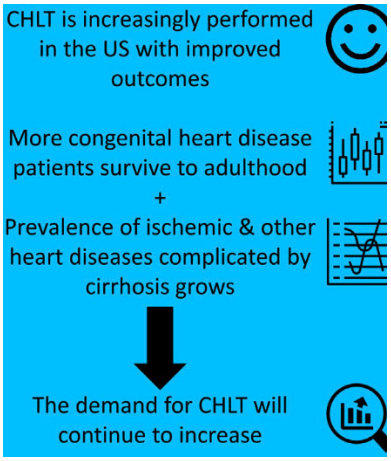
- Alexopoulos, et al. Transplant International. 2022,V35, article 10036
  - Summary



Era-related Changes in Cardiac Diagnosis

1989-2000	Restrictive/infiltrative
2001-2010	Restrictive/infiltrative
2011-2020	Congenital

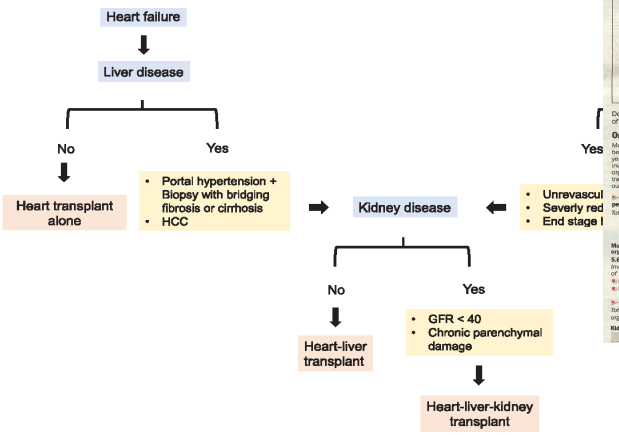
Patient Mortality

Recipient	
Age, MELD-XI, Cardiac Diagnosis	
Diabetes	aHR = $_{1.23}2.35_{4.48}$
Compared to 2011-2020	
1989-2000	aHR = $_{1.13}5.00_{22.26}$
2001-2010	aHR = $_{0.93}1.67_{3.00}$
Donor	
Age, Diabetes	
Left Ventricular EF	aHR = $_{0.92}0.96_{0.99}$
Compared to Sequential first	
Sequential first	aHR = $_{1.15}2.44_{5.18}$
Simultaneous	aHR = $_{0.42}1.39_{4.64}$

Heart - Liver - Kidney Transplant

Heart-Liver-Kidney Transplant

- First attempted by Starzl in 1989
- First successful at UCMC 1999
- Eligibility - Combining HT, HLT and HKT criteria



Doloros Slater is at the bedside of her husband, Kent, who, last week at the University of Chicago Hospitals, underwent the second heart-liver-kidney transplant ever performed.

Organ transplants

More transplants are being performed each year; operations typically involve only a single organ. The need for transplants continues to outpace available organs.

Transplants performed in 1998
Total transplants: 20,759

Single organ 94.4%

Multiple organ 5.6%
Involving two or three of these organs:
Kidney Liver
Pancreas Heart

On waiting list
Total requests for major organs: 66,831*

Kidneys 43,403

Saying he feels 'pretty good, considering,' a Michigan man is recovering after undergoing the 2nd heart-liver-kidney transplant ever. The procedure, however, has raised some ethical questions.

Lifesaving —times 3

By Jeremy Manier
Tribune Staff Writer

Kent Slater wobbled just a bit crossing the Chicago hand

phases of Slater's transplant. "We haven't changed his brain at all. But it is kind of a surrealistic phenomenon."

Chicago Tribune
5/14/99

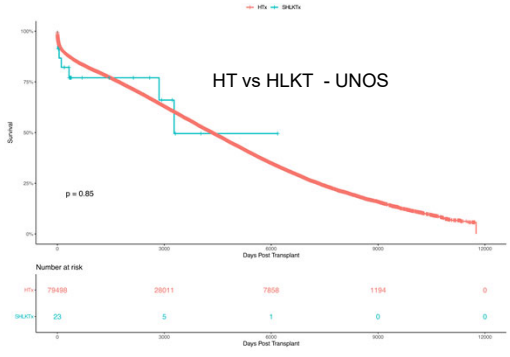
The university of TRANSPLANTATION WILEY

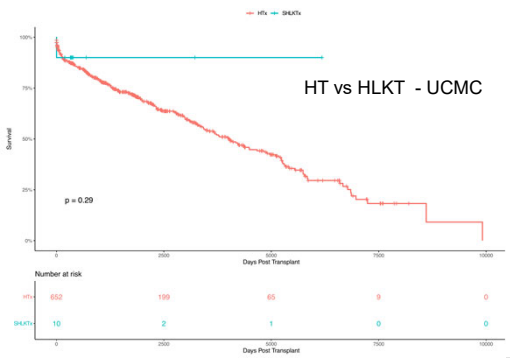
Aalok Kacha[4] | Valluvan Jeevanandam[2] | Yolanda Becker[1] | Lisa Potter[1] | Govind Rangrass[4] |
John [illegible][1] | Talia B. Baker[1]

Clinical Transplantation. 2022;e14586

Heart-Liver-Kidney Transplant

- Highly complex coordination
- Resources and time consuming
- Very low volumes (end of 2020) - 24 reported in UNOS; UCMC 12
- UCMC – 1 early mortality in 2003 from bleeding
- UCMC – 1 patient received delayed safety net kidney





University of Chicago Medicine

UCM Heart Transplant Program

- SRTR nationwide report (dates: 1/18 – 7/20)
- Best survival

Figure C16D. Adult (18+) 1-year patient death HR program comparison (deceased donor grafts)

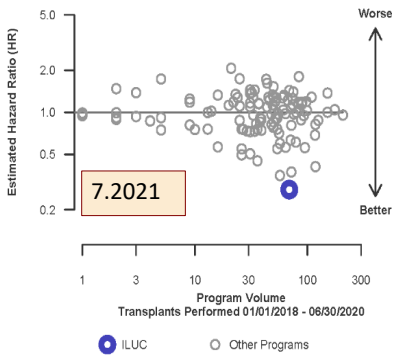
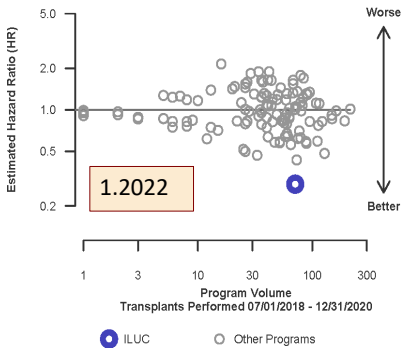


Figure C16D. Adult (18+) 1-year patient death HR program comparison (deceased donor grafts)



UCM Heart Transplant Program

- SRTR nationwide report (dates: 1/18 – 7/20)
- Best survival
- Shortest wait times

Table B10. Time to transplant for waiting list candidates*
Candidates registered on the waiting list between 01/01/2015 and 06/30/2020

7.2021

Percentile	Months to Transplant** Center	OPO/DSA	Region	U.S.
5th	0.2	0.2	0.3	0.2
10th	0.2	0.4	0.4	0.4
25th	0.5	1.1	1.6	1.2
50th (median time to transplant)	1.1	5.6	9.5	6.2
75th	2.8	Not Observed	Not Observed	Not Observed

Table B10. Time to transplant for waiting list candidates*
Candidates registered on the waiting list between 07/01/2015 and 12/31/2020

1.2022

Percentile	Months to Transplant** Center	OPO/DSA	Region	U.S.
5th	0.1	0.2	0.2	0.2
10th	0.2	0.3	0.4	0.3
25th	0.4	1.0	1.3	1
50th (median time to transplant)	0.9	4.5	7.4	5.5
75th	2.5	Not Observed	Not Observed	Not Observed

UCM Heart Transplant Program

- SRTR nationwide report (dates: 1/18 – 7/20)
- Best survival
- Shortest wait times
- Highest transplant rate
- 25% of patients referred from other txn programs
  - Complex congenital
  - Highly sensitized
- Most bloodless patients
  - Jehovah's Witnesses
- Most heart/liver/kidneys
  - 13/25 done in the history of the USA
  - Best survival of any program

AT THE FOREFRONT UChicago Medicine | Heart & Vascular Center

Heart Transplant Program
- The Best in the USA
- *De facto* The Best in the World

Multiple Organ Heart Transplantation

- HL, HK, HLK performed with excellent results
- Highest status organ pulls other
  - Forced sharing within 500 miles will help
- Survival equivalent or better than HT alone
- Dedicated, daring Team
- Needs tremendous coordination and institutional commitment
- High risk, high resource utilization and so rewarding