What should nephrologists know about multi-organ transplant candidates?

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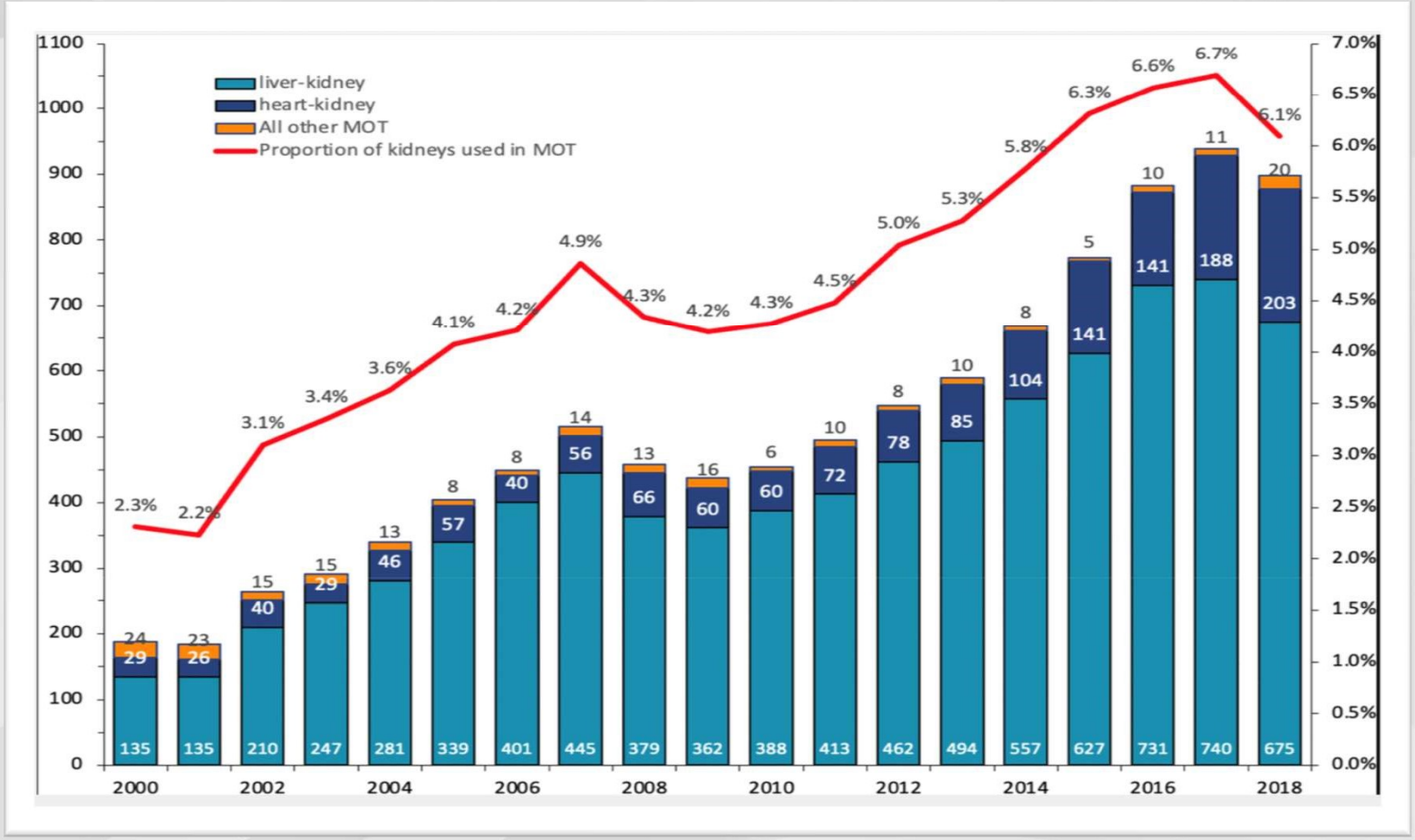
Tbilisi State Medical University,
13-14 September, Tbilisi, 2023

Outline

1. Impact of pre-transplantation renal dysfunction on MOT outcomes
2. Assessment of pre-MOT renal dysfunction
3. Approach to patient selection for simultaneous liver-kidney/heart-kidney (SLK/SHK) transplantation
4. Explore the ethics of multiorgan transplantation

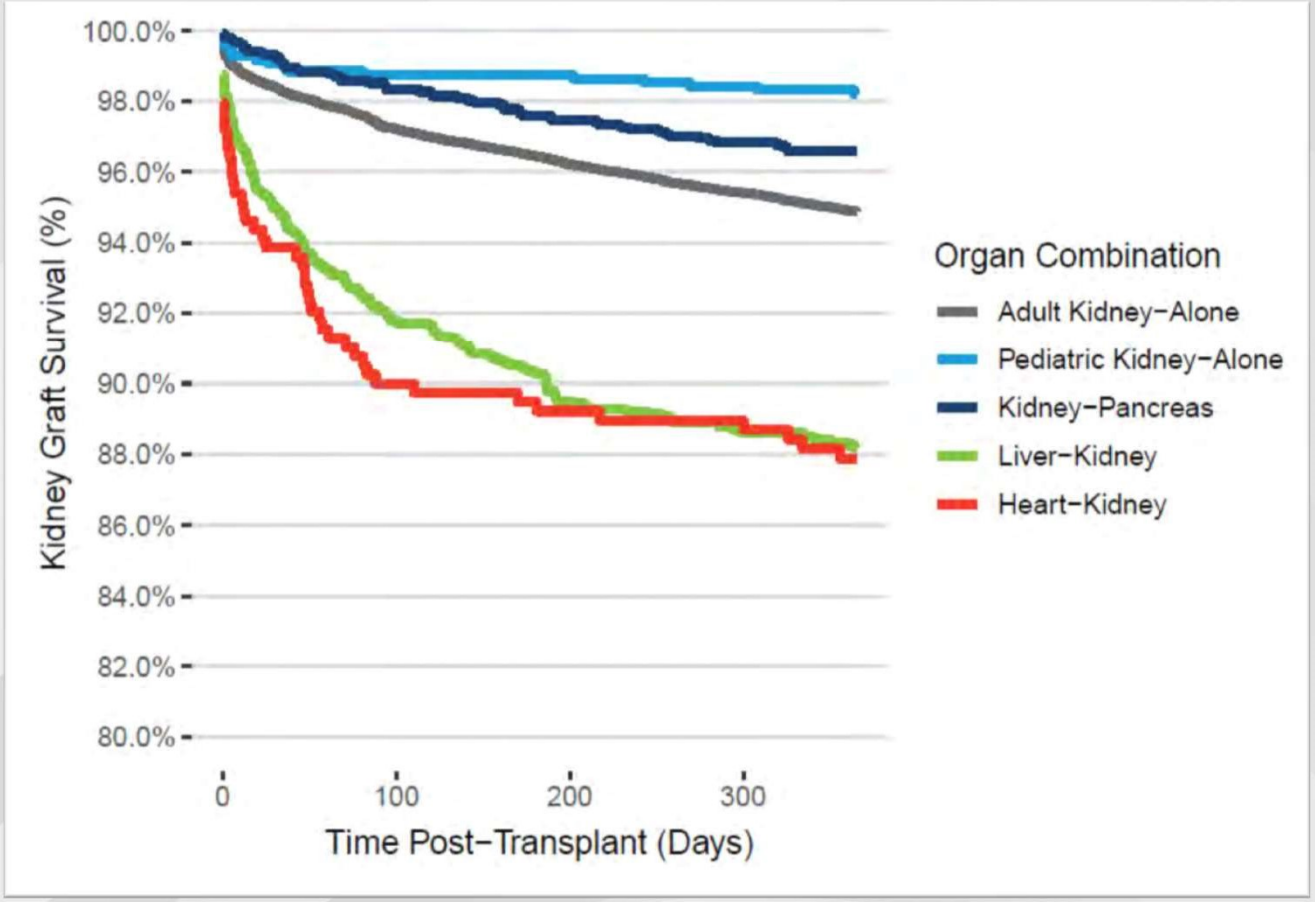
Increasing number of multiorgan transplants per year and proportion of kidneys used



Simultaneous heart-kidney transplatation SHK

Simultaneous liver-kidney transplatation SLK

One-Year Post Transplant Kidney Graft Survival by Organ Combination, 2017-2018



Rashikh A et al. *Transplantation* no. 101 (2017): 368-376

Examining Kidney Priority for Multi-Organ Candidates Compared to Pediatric Kidney-Alone Candidates," OPTN.

AJKD AMERICAN JOURNAL OF KIDNEY DISEASES

NATIONAL KIDNEY FOUNDATION®

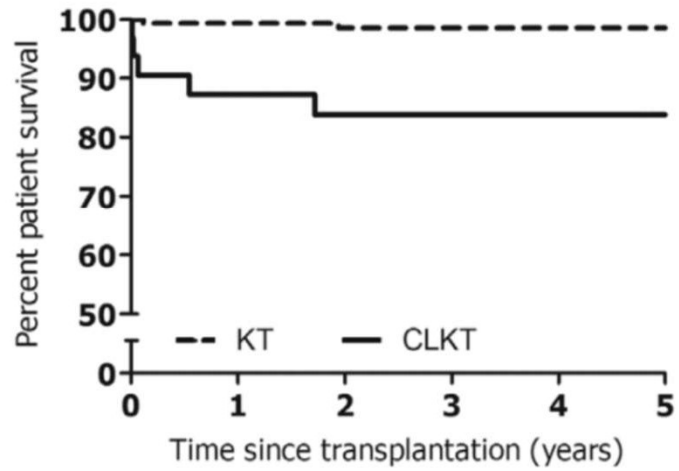
Kidney Versus Combined Kidney and Liver Transplantation in Young People With Autosomal Recessive Polycystic Kidney Disease: Data From the European Society for Pediatric Nephrology/European Renal Association - European Dialysis and Transplant (ESPN/ERA-EDTA) Registry

The data for children, adolescents, and young adults with ARPKD with either kidney or combined liver-kidney transplants 1995 - 2012 from the ESPN/ERA-EDTA Registry

202 patients with ARPKD aged 19 years or younger
HD duration - median of 0.4 (IQR, 0.0-1.4) years

Age - median 9.0 (IQR, 4.1-13.7) years
32 (15.8%) SLK
163 (80.7%) KAT

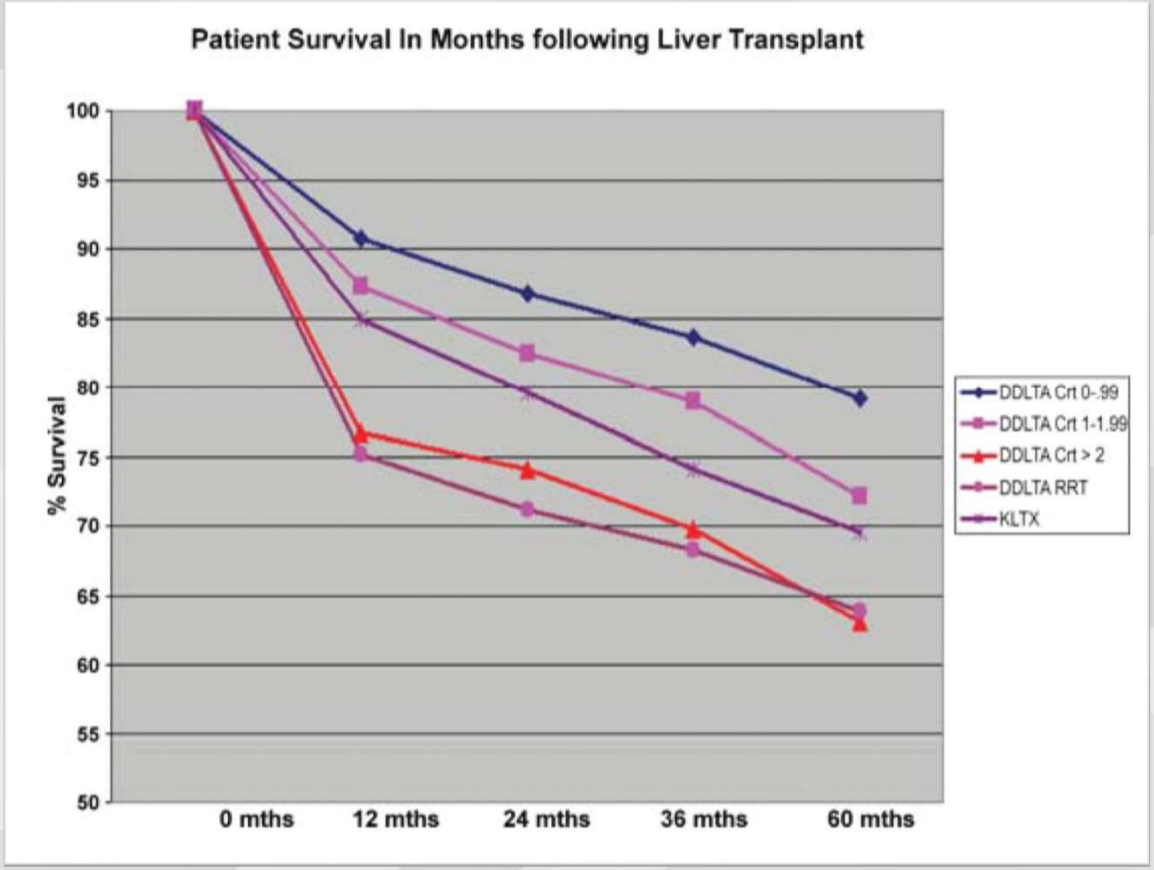
Age- and sex-adjusted 5-year patient survival:
87.0% (95% CI, 75.8%-99.8%) - SLK
97.4% (95% CI, 94.9%-100.0%) - KAT



Number of patients at risk						
KT	163	137	119	101	84	68
CLKT	32	27	21	18	16	11

Djalila Mekahli, MD et al. Am J Kidney Dis. 2016;68(5):782-788

Impact of renal function on postliver transplant survival



Variable	p-Value	RR	95% CI
DDLTA-Crt 1–1.99 versus DDLTA Crt < 1	0.0461	1.11	[1.00, 1.23]
DDLTA-Crt>2 versus DDLTA < 1	<0.0001	1.58	[1.36, 1.83]
DDLTA-RRT versus DDLTA Crt < 1	<0.0001	1.77	[1.47, 2.13]
KLTX versus DDLTA-Crt < 1	0.0004	1.44	[1.18, 1.76]

SLK - better survival in patients on KRT and marked kidney dysfunction

Gonwa TA et al. *Am J Transplant.* 2006;6:2651–2659

Renal function in liver disease and predictors of renal recovery after LAT

Simultaneous Liver Kidney Transpalnation

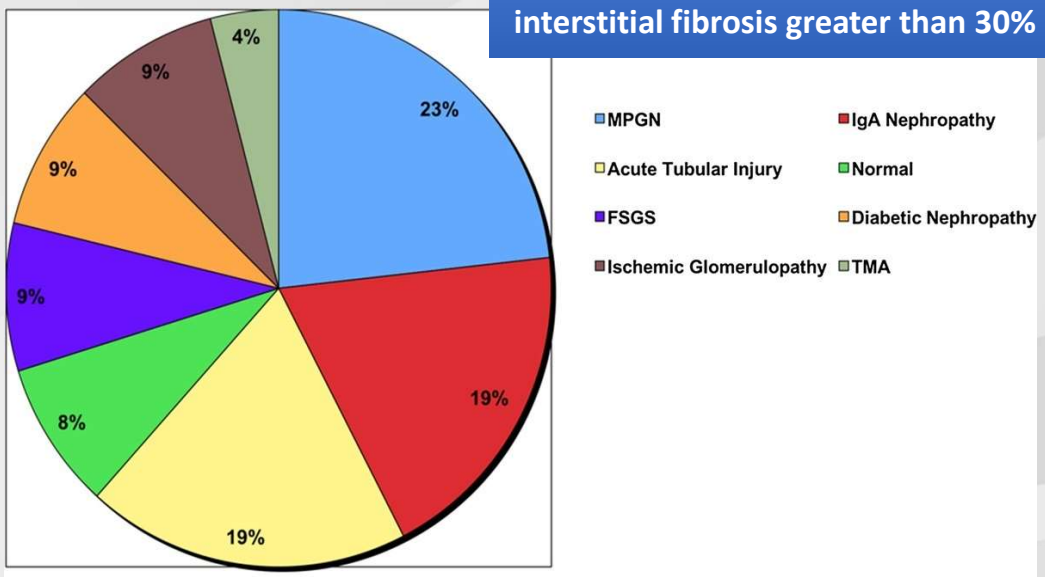
Liver alone?

Assays for Evaluation of Kidney Function

- SCr and SCr-based race-free eGFR equation; CKD-EPI refit without the race variable
- CysC and CysC/SCr-based eGFR equations (not enough evidence in MOT candidates)
- 24-h creatinine/urea clearance (insufficient data in MOT candidates)
- Kidney ultrasound (High interoperator and interreader variability)
- Kidney biopsy (risk of bleeding)

Kidney Biopsies May Help Predict Renal Function Recovery After Liver Transplantation

SLK recommended:
to greater than 40% global GS, with interstitial fibrosis greater than 30%



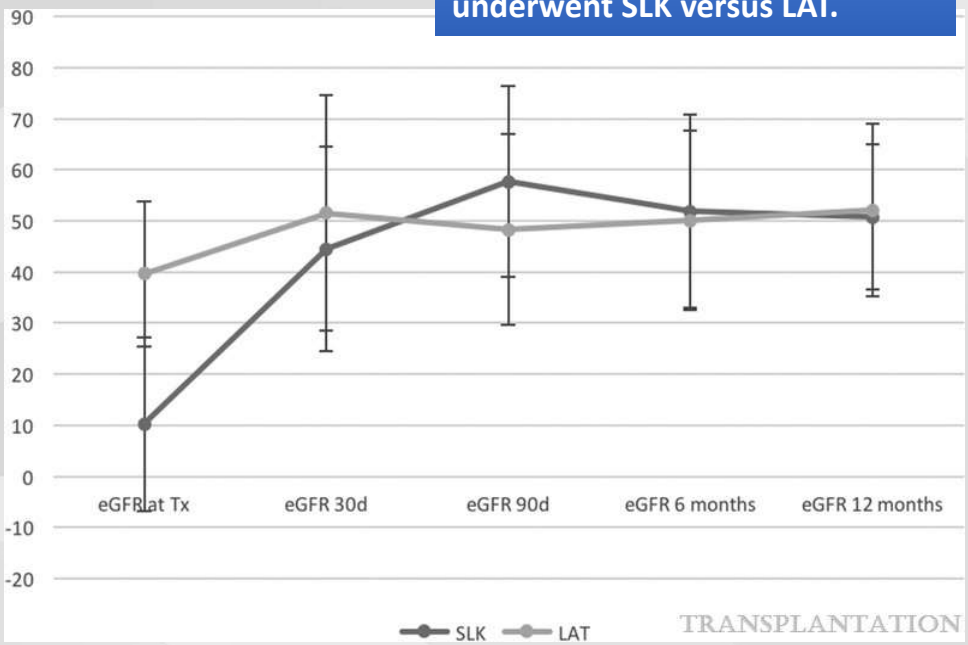
Abbreviations: MPGN=membranoproliferative Glomerulonephritis; FSGS=Focal Segmental Glomerulosclerosis; TMA=Thrombotic Microangiopathy

TRANSPLANTATION

Pichler, Raimund H et al.
Transplantation100(10):2122-2128, October 2016.

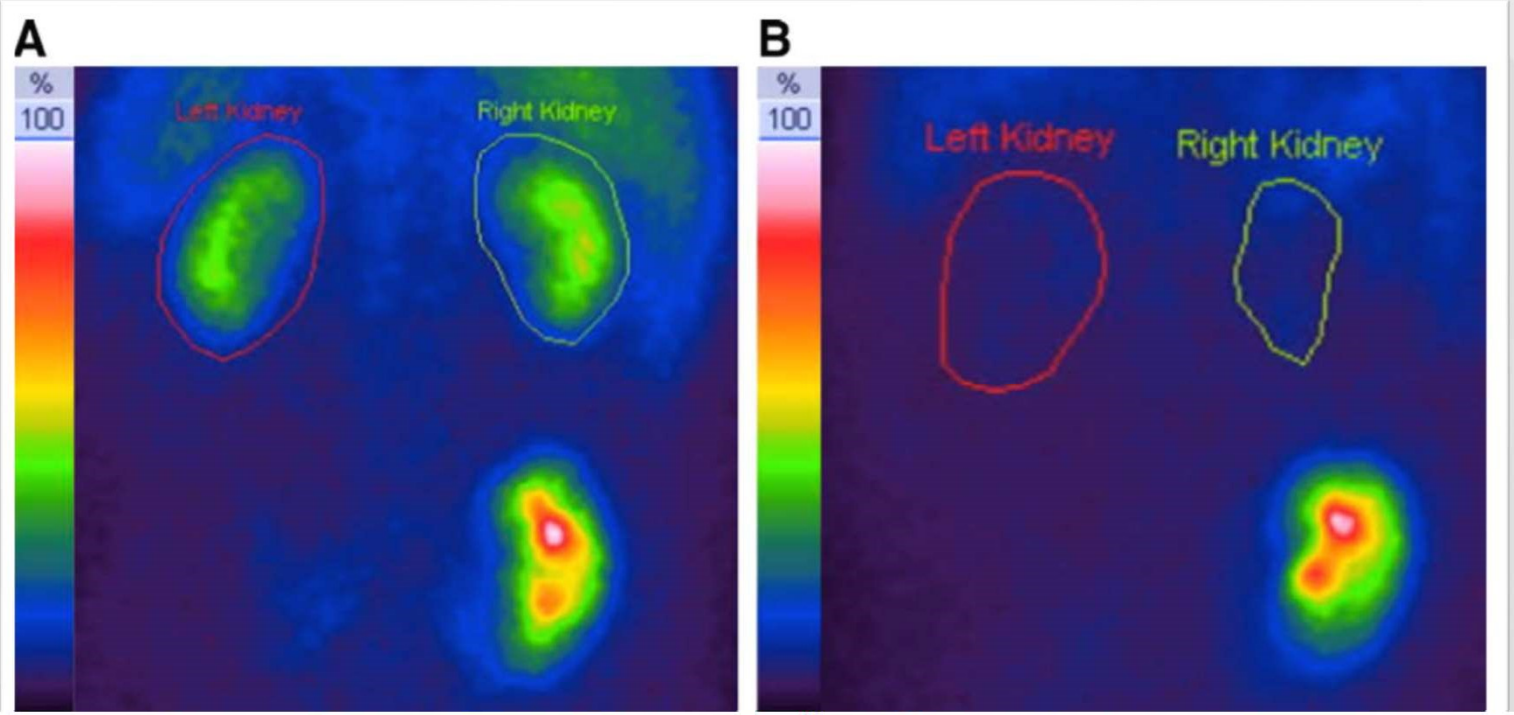
Wolters Kluwer

Average pre- and pos-tliver transplant eGFRs in patients who underwent SLK versus LAT.



Avoided kidney allocation to 70% of LT candidates

Assessment of Native Kidney Function Recovery With Renal Scintigraphy Following Simultaneous Liver-Kidney Transplantation



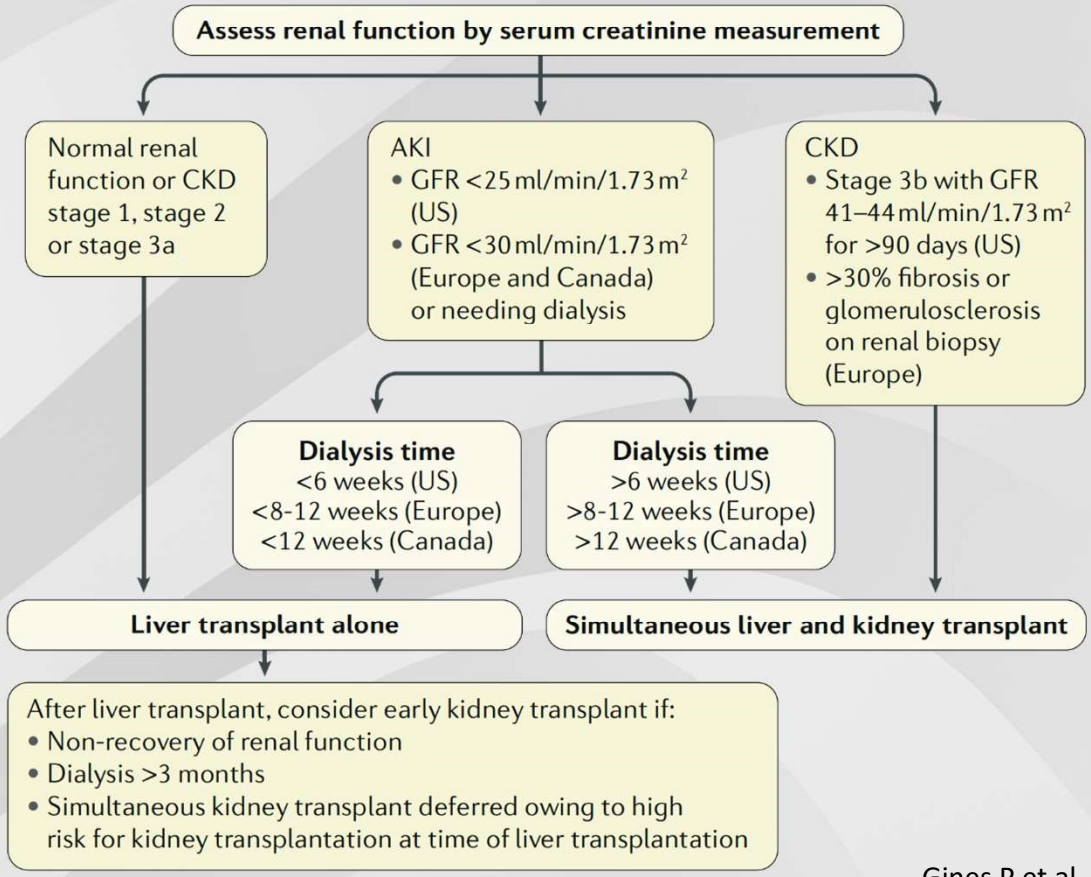
Kidney function of patients who underwent SLK followed by ^{99m}Tc-MAG3 renal scintigraphy[a]

	Kidney function 90 d before SLK[b]	Kidney function at SLK[b]	Overall kidney function at sCr nadir	Contribution of native kidneys at sCr nadir	Contribution of renal allograft at sCr nadir
eGFR[c] (SD)	23.1 (14.6)	14.2 (8.6)	88.7 (25.5)	44.5 (15.8)*	44.2 (19.2)*

*$P < 0.0001$.

Werneburg, Glenn T.et al. Transplantation 107(2):p 540-547, February 2023

Algorithm for liver transplant alone versus simultaneous liver and kidney transplant in HRS.

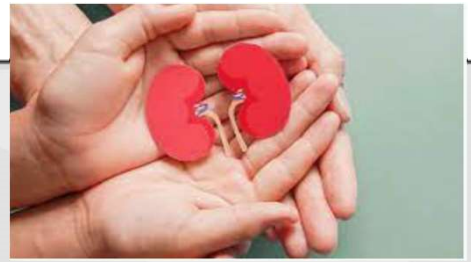


Gines P et al, Nature Reviews Disease Primers 2018

Hepatocentric vs Nephrocentic approaches to kidney transplantation in patients with liver failure

Hepatocentric Approach—Prefer SLK	Nephrocentric Approach—Prefer LTA
(1) SLK will maximize the graft and patient survival of liver transplant recipients	(1) Patients with pure hepatorenal syndrome should completely recover renal function after LTA
(2) Liver transplant patients often need a kidney transplant anyway	(2) For such patients, kidney transplantation is completely unnecessary and has associated risks
(3) Receiving SLK avoids time on dialysis and impact on morbidity, mortality, and subsequent kidney graft survival.	(3) Every kidney used for a patient with SLK cannot be used for a patient >with ESRD. This lengthens the waiting time for renal transplantation, thus worsening mortality for ESRD patients
(4) SLK reduces immunological risk compared to kidney transplant after LTA, because the liver and kidney are from same donor	(4) SLK patients get the best quality kidneys, thus making them unavailable for patients with ESRD
(5) Kidney transplantation after LTA has poor outcomes	(5) Kidney transplant recipients after LTA have comparable patient survival to kidney only recipients.
(6) There is no harm in having a third kidney provide more kidney function	

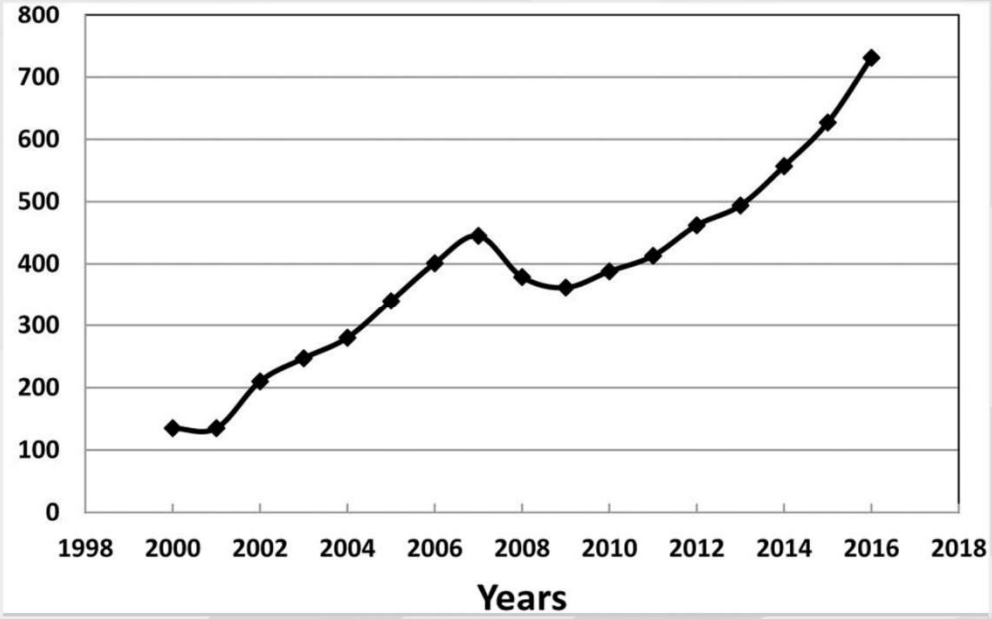
TRANSPLANTATION



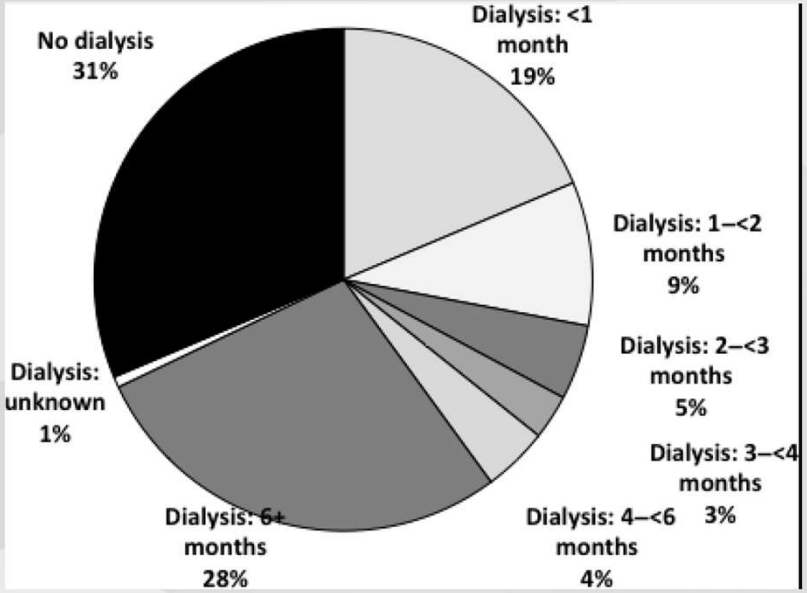
Wolters Kluwer

Parajuli, Sandesh et al. Transplantation99(9):1756-1764, September 2015.

Need for refining of Simultaneous Liver Kidney Transplantation policy



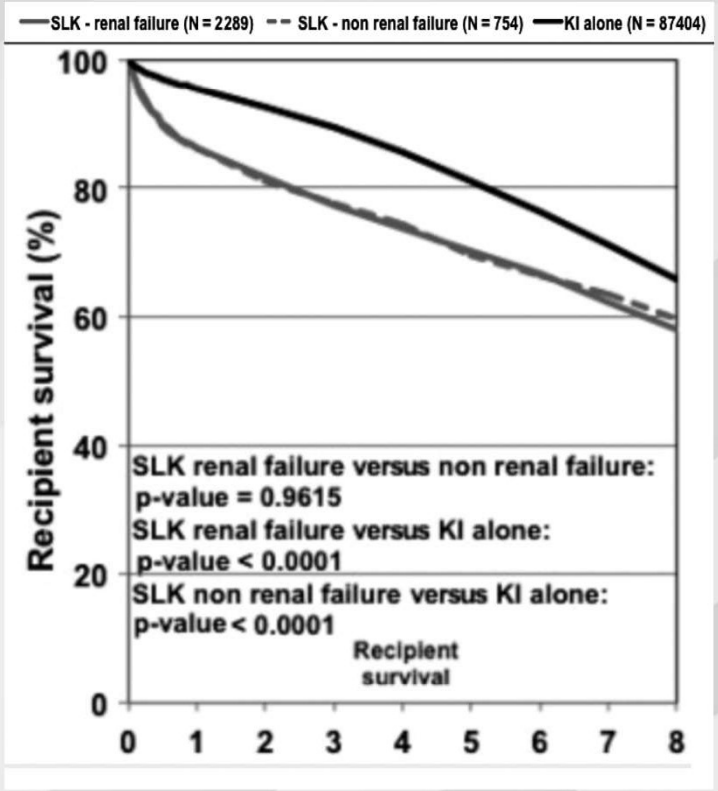
Introduction of MELD scoring in 2002 increase SLK numbers

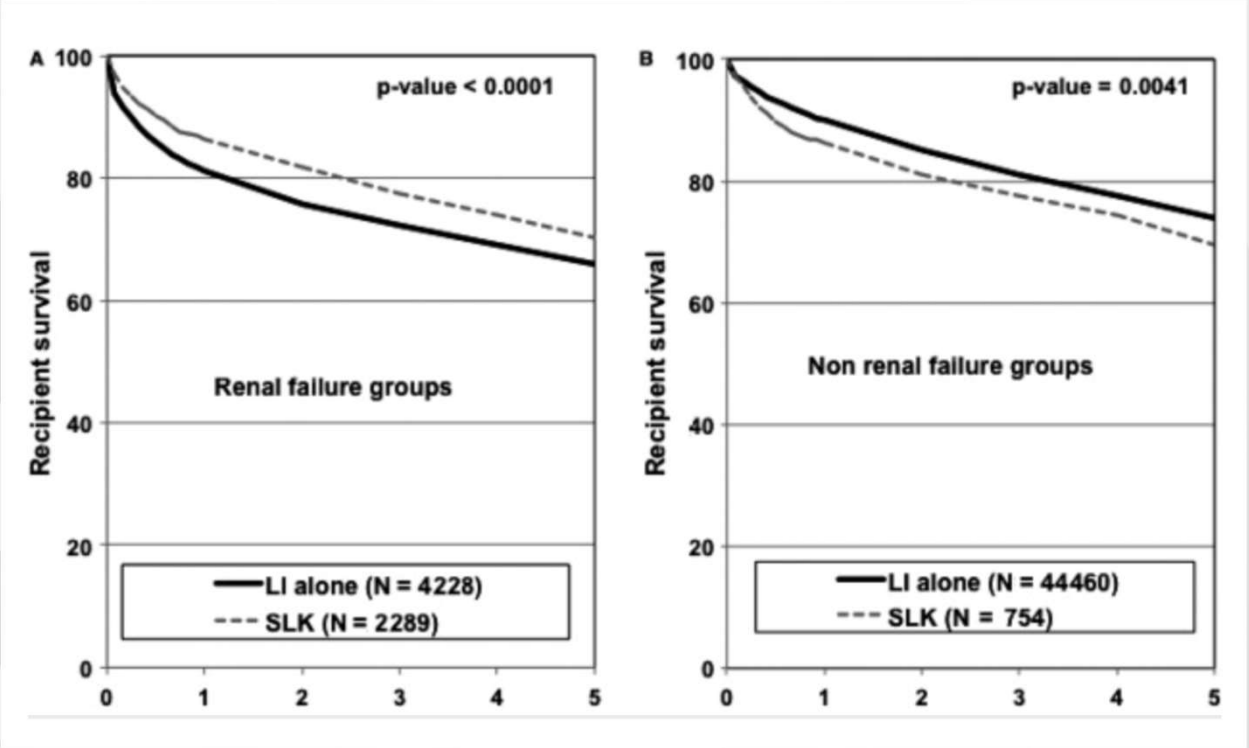


SLK transplant
48.3% of donors with a KDPI <0.35
31% of SLK recipients no dialysis prior SLK
22% < 2 mo of dialysis

Formica RN et al. *Am J Transplant.* 2016;16:758–766.

Comparison of outcomes after SLK vs LTA with and without marked kidney dysfunction





pretransplant dialysis time of >2 months or serum creatinine >2.5 mg/dL

Formica RN et al. *Am J Transplant.* 2016;16:758–766.

OPTN | UNOS Public Comment Proposal

OPTN/UNOS Kidney Transplantation Committee

Simultaneous Liver Kidney (SLK) Allocation Policy

SLK Medical Eligibility Criteria

If the candidate's transplant nephrologist confirms a diagnosis of:	Then the transplant program must document in the candidate's medical record:
Chronic kidney disease (CKD) with a measured or calculated glomerular filtration rate (GFR) less than or equal to 60 mL/min for greater than 90 consecutive days	At least one of the following: • That the candidate has begun regularly administered dialysis as an end-stage renal disease (ESRD) patient in a hospital based, independent non-hospital based, or home setting. • At the time of registration on the kidney waiting list, that the candidate's most recent GFR or measured or estimated creatinine clearance (CrCl) is less than or equal to 30 mL/min. • On a date after registration on the kidney waiting list, that the candidate's GFR or measured or estimated CrCl is less than or equal to 30 mL/min.
Sustained acute kidney injury	At least one of the following, or a combination of both of the following, for the last 6 weeks: • That the candidate has been on dialysis at least once every 7 days. • That the candidate has a GFR or measured or estimated CrCl less than or equal to 25 mL/min at least once every 7 days. If the candidate's eligibility is not confirmed at least once every seven days for the last 6 weeks, the candidate is not eligible to receive a liver and a kidney from the same donor.
Metabolic disease	An additional diagnosis of at least one of the following: 1. Hyperoxaluria 2. Atypical HUS from mutations in factor H and possibly factor I 3. Familial non-neuropathic systemic amyloid 4. Methylmalonic aciduria

Safety net: Match classification priority for liver recipients by KDPI sequence

Sequence A KDPI ≤ 20%	Sequence B KDPI >20% but <35%	Sequence C KDPI >35% but <85%	Sequence D KDPI >85%
Highly sensitized	Highly sensitized	Highly sensitized	Highly sensitized
0-ABDR mismatch	0-ABDR mismatch	0-ABDR mismatch	0-ABDR mismatch
Prior living donor	Prior living donor	Prior living donor	Local SLK safety net
Local pediatrics	Local pediatrics	Local SLK safety net	Local +regional
Local top 20% EPTS	Local SLK safety net	Local candidates	National candidates
0-ABDR mismatch (all)	Local adults	Regional candidates	
Local (all)	Regional pediatrics	National candidates	
Regional pediatrics	Regional adults		
Regional (top 20%)	National pediatrics		
Regional (all)	National adults		
National pediatrics			
National (top 20%)			
National (all)			

Developing simultaneous liver-kidney transplant medical eligibility criteria while providing a safety net: A 2-year review of the OPTN's allocation policy

What were the early impacts of the 2017 simultaneous liver-kidney transplant allocation policy?

OPTN data analysis

Simultaneous liver-kidney Tx (SLK)

Kidney after liver Tx (KAL)

Pre-policy vs Post-policy

Assess:

Tx volume/rates, waitlist mortality, patient/graft survival

SLK policy implementation interrupted the longstanding rise in SLK transplants

The Safety Net provision directed kidneys to liver recipients in need, with minimal impact to postTx outcomes

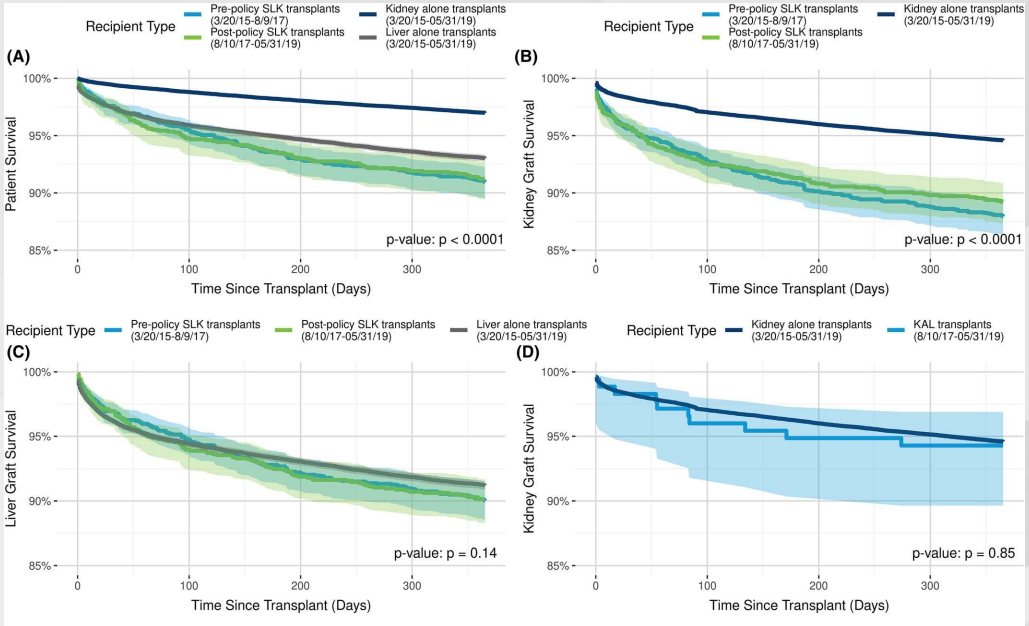
AJT

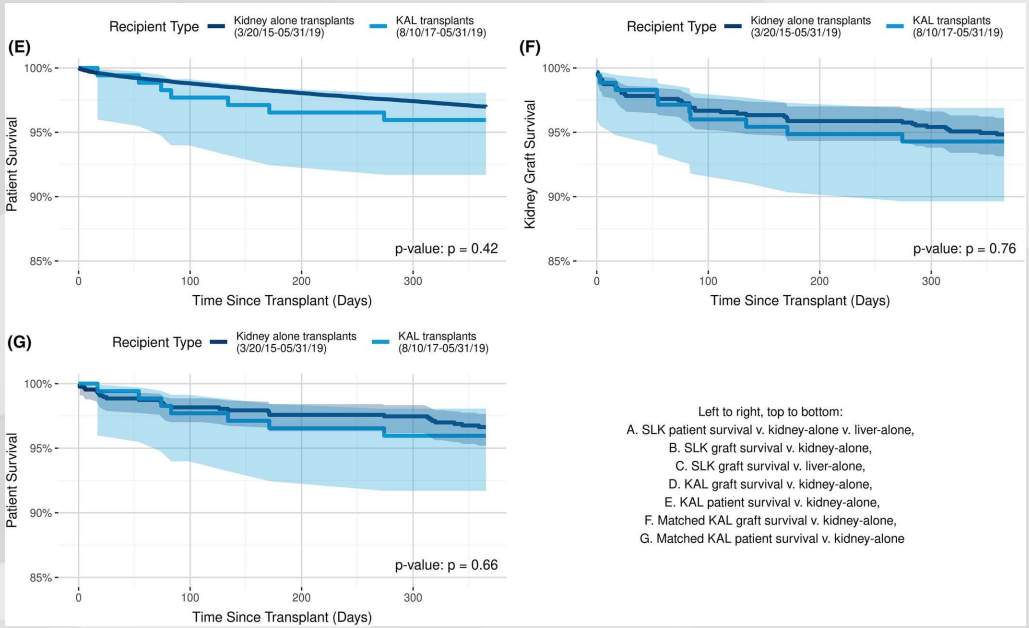
Wilk et al

Created by the AJT Editorial Office

10.1111/ajt.16761

Developing simultaneous liver-kidney transplant medical eligibility criteria while providing a safety net: A 2-year review of the OPTN's allocation policy



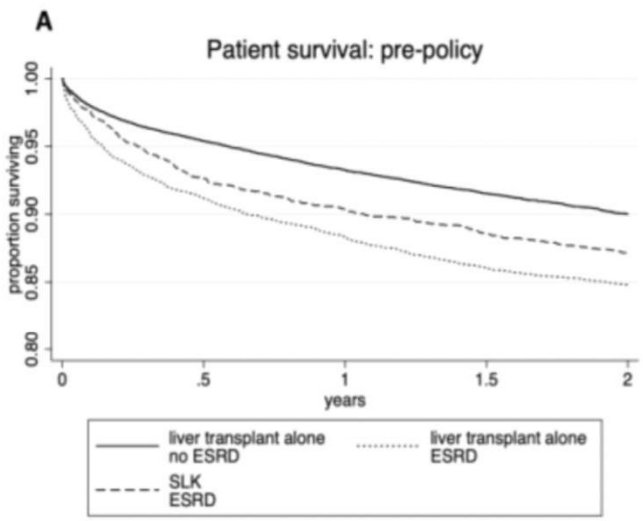


American J Transplantation, Volume: 21, Issue: 11, Pages: 3593-3607,
First published: 13 July 2021, DOI: (10.1111/ajt.16761)

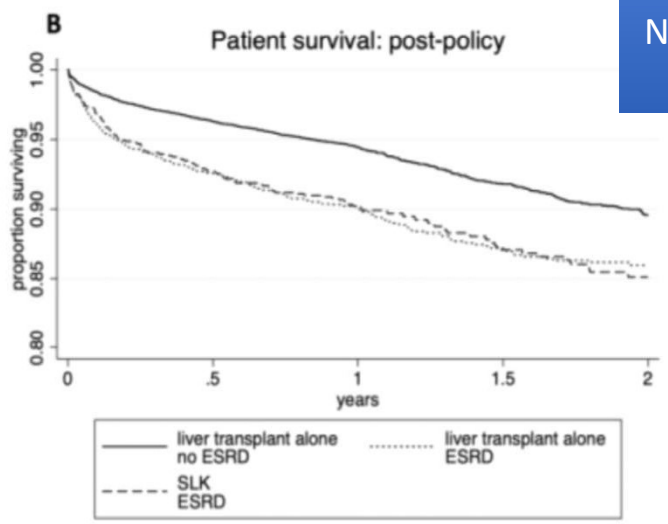
SLK policy impact on patiens outcome

Among patients with kidney failure

NO difference in patient's survival SLK vs. LA

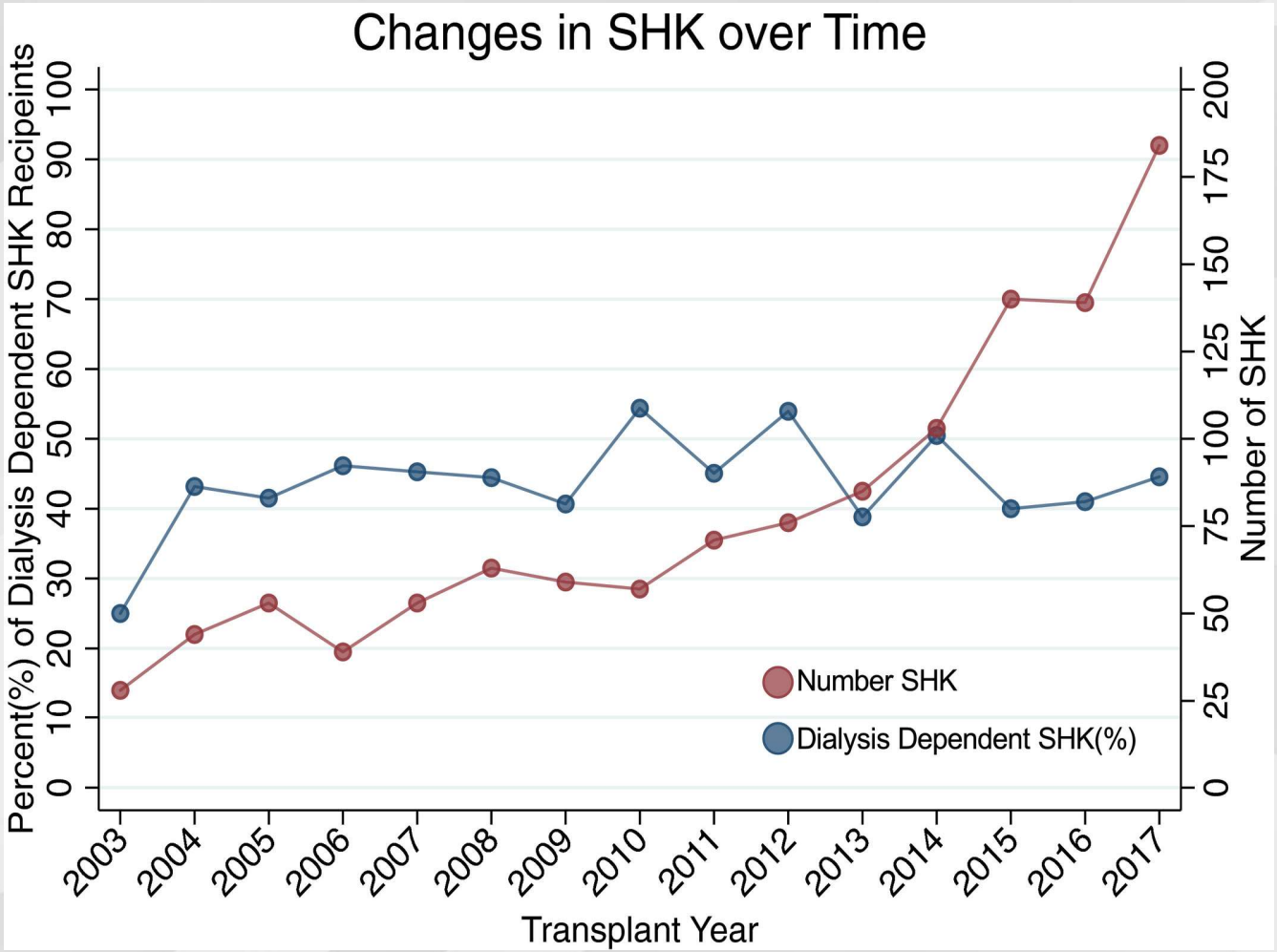


	Patient Survival (95% CI)	
	1 year	2 years
LTA no ESRD	0.93 (0.92-0.93)	0.88 (0.87-0.89)
LTA ESRD	0.87 (0.86-0.88)	0.84 (0.81-0.86)
SLK ESRD	0.90 (0.89-0.91)	0.87 (0.86-0.88)



	Patient Survival (95% CI)	
	1 year	2 years
LTA no ESRD	0.93 (0.92-0.94)	0.89 (0.88-0.89)
LTA ESRD	0.87 (0.86-0.89)	0.83 (0.81-0.85)
SLK ESRD	0.88 (0.86-0.90)	0.84 (0.81-0.86)

Samoylova ML, et al. Liver Transpl 27: 1106–1115



four-fold increase in SHK 1.6% to 6.6% of total hearts transplanted

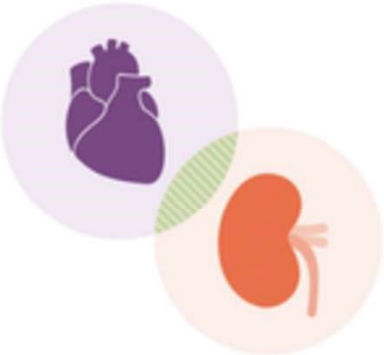
Proportion of dialysis-dependent patients with SHK unchanged

Shaw BI et al. Am J Transplant. 2021 Jul;21(7):2468-2478.

Impact of pretransplant eGFR on SHK outcome

Need for improvements in simultaneous heart-kidney allocation: The limitation of pretransplant glomerular filtration rate

What are the trends and outcomes for simultaneous heart-kidney transplantation (SHK)?



Retrospective study
SRTR data 2003–2017

- Quantify changes in the practice of SHK
- Examine the survival of SHK vs heart-alone Tx
- Identify patients with marginal benefit from SHK

Incidence of SHK increased (1.6⇨6.6%)

SHK was associated with increased survival in dialysis-dependent patients

Increasing eGFR diminished SHK impact on reducing hazard of death

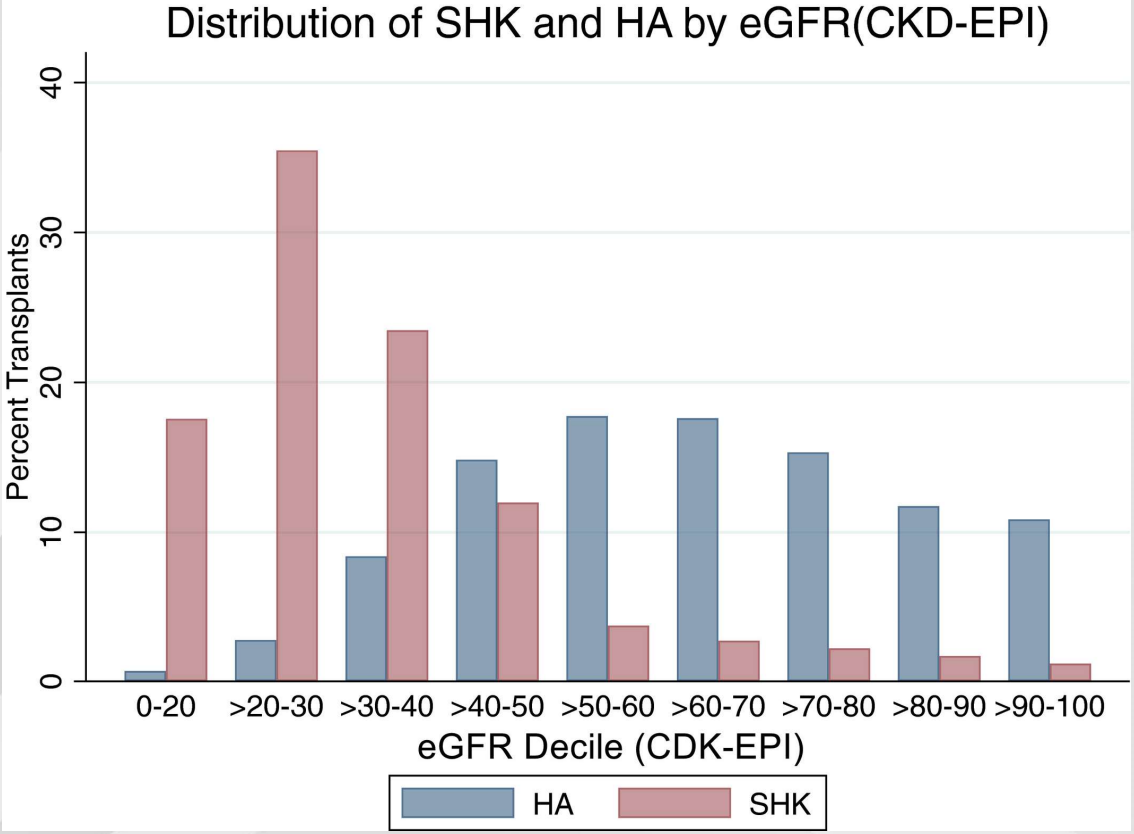
26% of SHK recipients had delayed graft function

AJT

Shaw et al

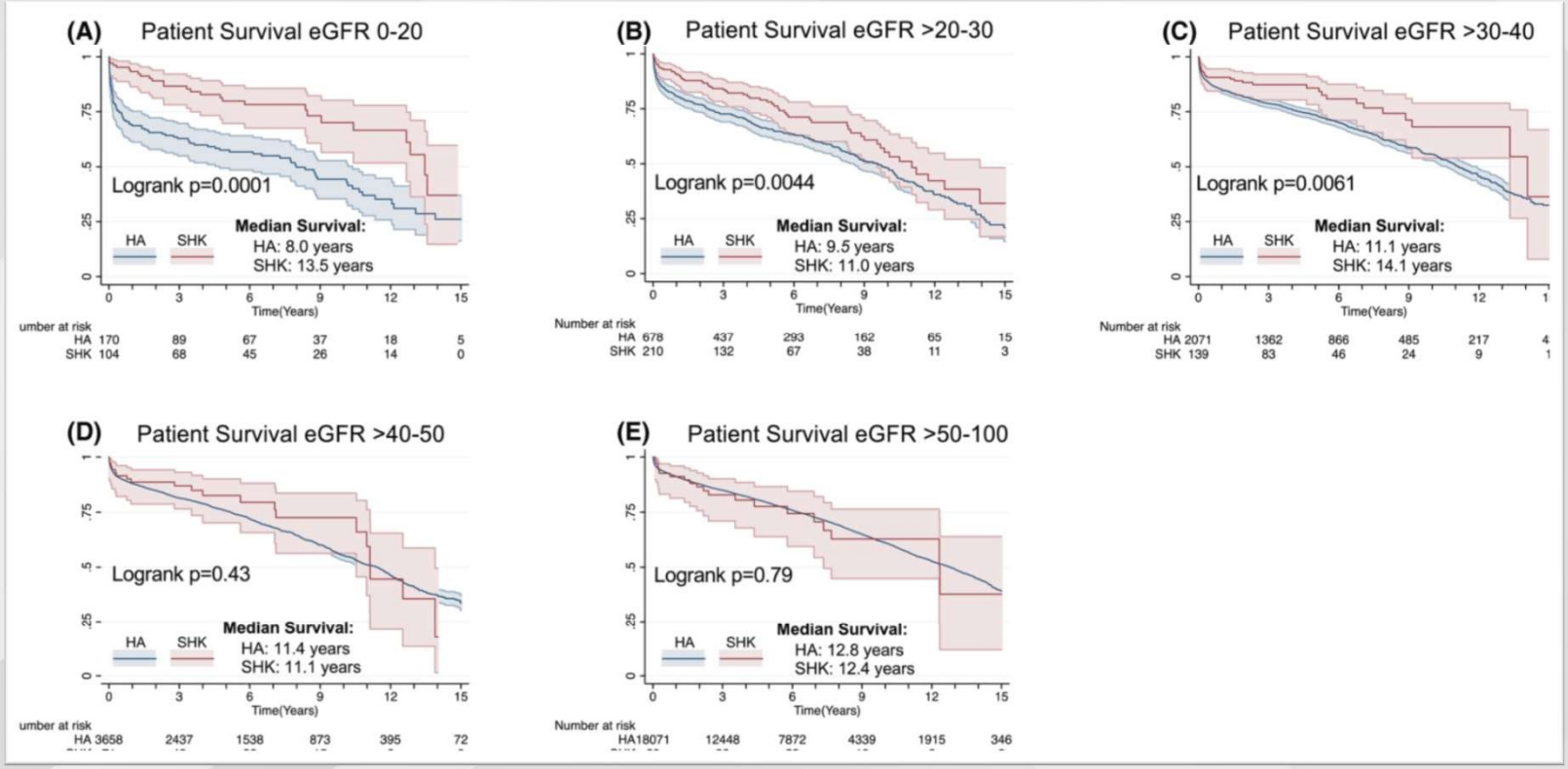
10.1111/ajt.16466

Proportion of HA and SHK transplants by eGFR



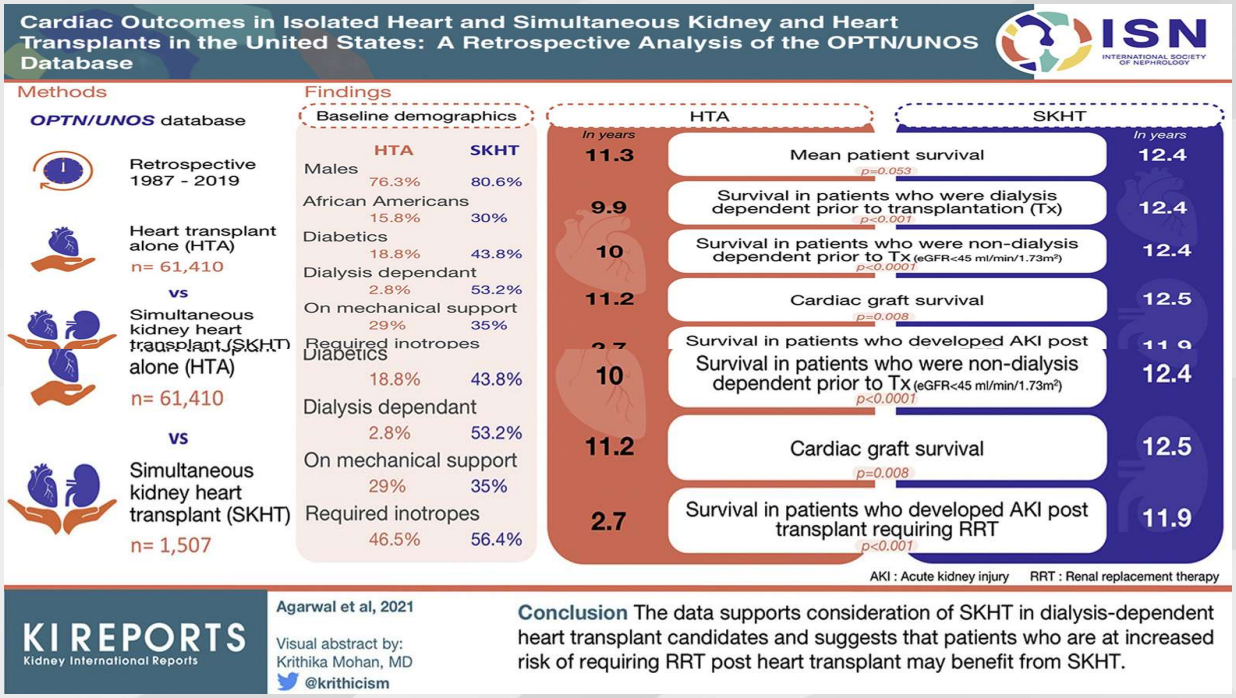
American J Transplantation, Volume: 21, Issue: 7, Pages: 2468-2478, First published: 22 December 2020, DOI: (10.1111/ajt.16466)

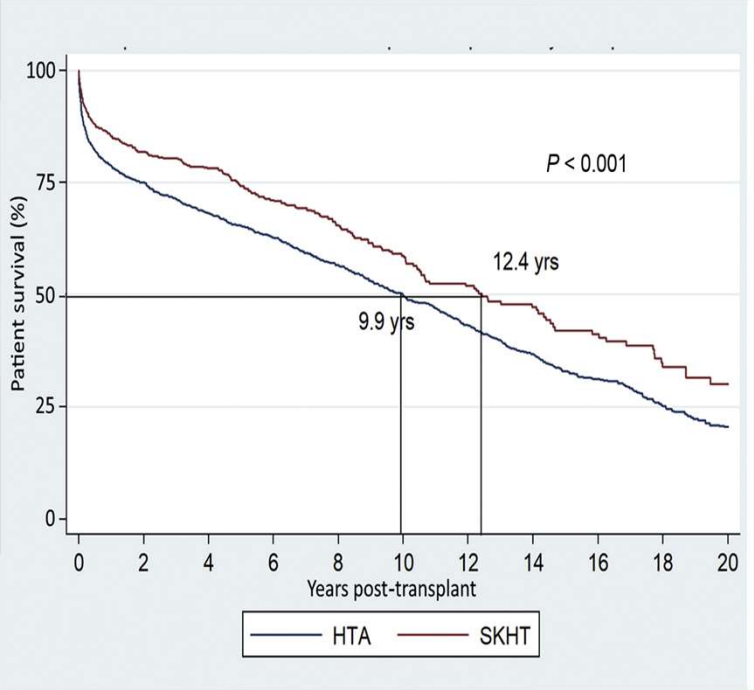
The association of SHK with survival is inversely correlated with eGFR



American J Transplantation, Volume: 21, Issue: 7, Pages: 2468-2478, First published: 22 December 2020, DOI: (10.1111/ajt.16466)

Who may benefit more from simultaneous kidney heart transplantation?





Proposed algorithm for heart-kidney transplantation consideration

Assess Renal Function
- **Ensure steady state/euvolemia/hemodynamic optimization**
- **Review baseline kidney function 3-12 months prior**
- **Screen with SCr, eGFR, and proteinuria**
- **Confirm with 24-h CrCl**

GFR <30 mL/min/1.73 m2 for >90 d → Consider Heart-Kidney Transplant

GFR 30-40 mL/min/1.73 m^2 → Consider:
- Intrinsic disease (DM, hypertension)
- Chronicity
- Ultrasound, proteinuria, FEUrea
- Impact of cardiac optimization

→ Intrinsic disease + not reversible → Consider Heart-Kidney Transplant

→ No intrinsic disease + reversible → Heart Transplant

GFR >40 mL/min/1.73 m^2 → Heart Transplant → eGFR 520 mL/min/1.73 m^2 post-HT day between 60 and day 365 → Kidney Transplant: Living Donor vs Safety Net

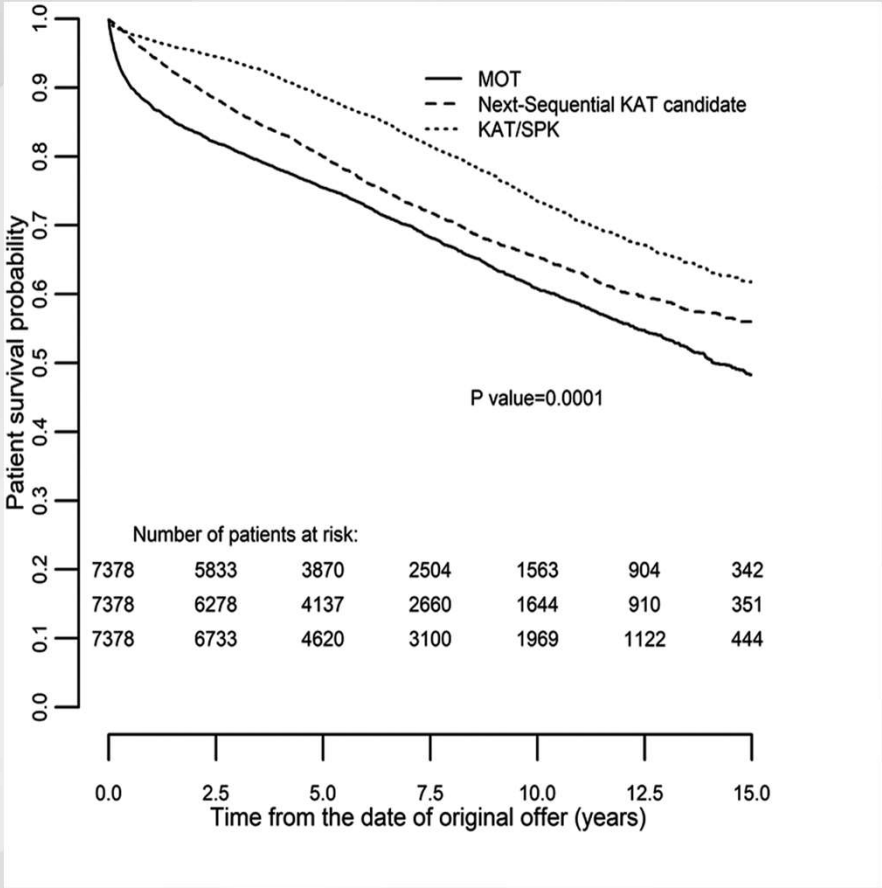
Kittleson M et al. Circulation, 2023;148:622–636

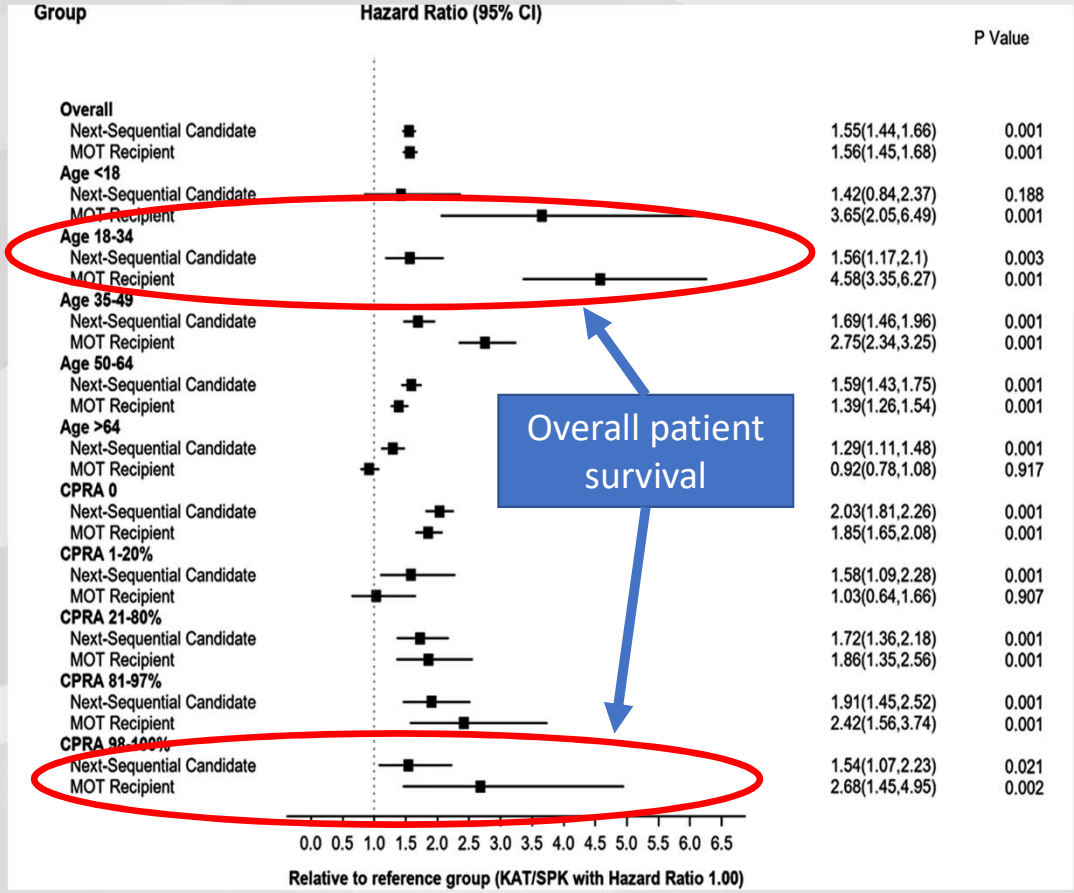
OPTN

Notice of OPTN Policy Changes

Establish Eligibility Criteria and Safety Net for Heart-Kidney and Lung-Kidney Allocation

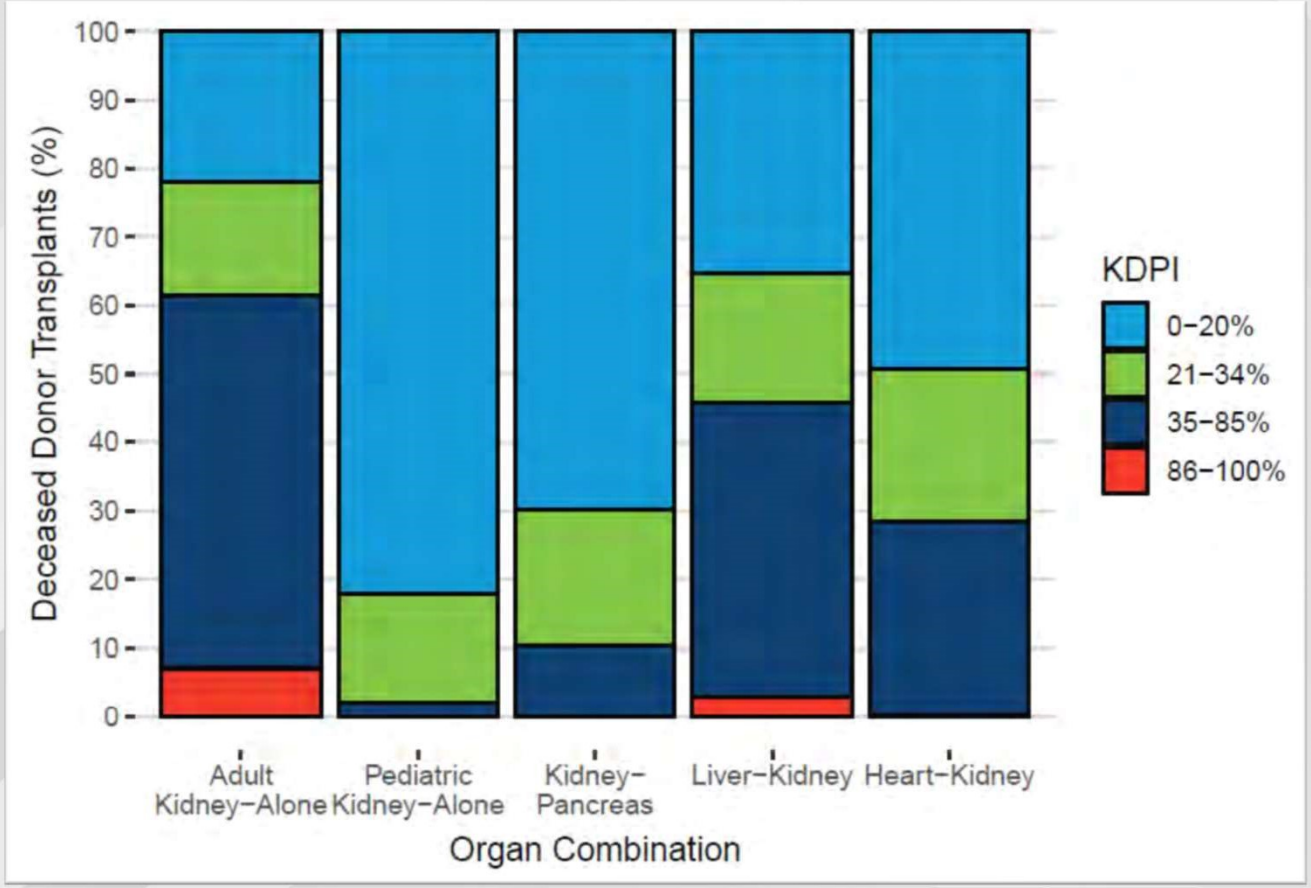
Impact of MOT on Kidney Candidate Survival





Westphal SG et al. Am J Transplant. 2021, Jun;21(6):2161-2174

Impact of MOT on kidney graft quality



S. Ali Husain, Kristen L. King, Geoffrey K. Dube, et al.,
Progress in Transplantation no. 29 (2019) 4: 354-360, DOI: 10.1177/1526924819874699.

OPTN

Concept Paper

Identify Priority Shares in Kidney Multi-Organ Allocation

OPTN Ad Hoc Multi-Organ Transplantation Committee

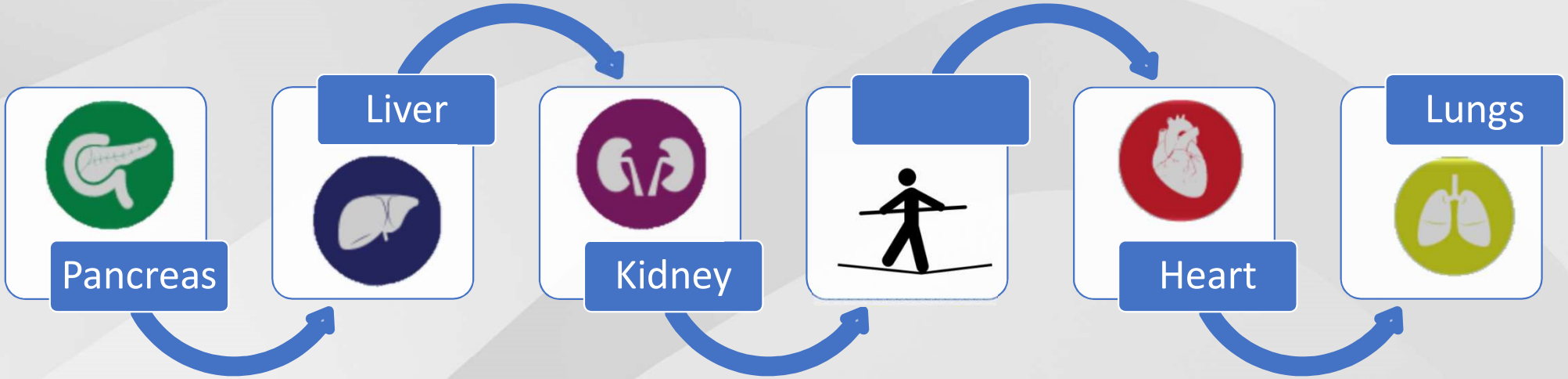
Framework for kidney multi-organ allocation to improve equity in access to transplant between single organ and multi-organ candidates, and to improve efficiency in allocating multiple organ types from one donor

1. If and when kidneys should be offered to kidney-alone candidates prior to kidney multi-organ candidates

2. How to determine which kidney (including laterality) should be offered to various kidney multi-organ and single organ candidates, many of whom have equal priority for offers in current policy

3. How to handle situations in which organ offer acceptance conflicts with a multi-organ offer required by policy

4. Providing more direction for multi-organ allocation while leaving flexibility for the dynamics of the allocation process



We need more evidence to "walk the tightrope"

Thank you!