Considerations for the Utilization of High KDPI Kidneys

August, 5, 2020
Meeting Reminders:

• Please mute your phone when not speaking to avoid background noise

• Be present and engaged

• Be prepared for active participation and open discussion

• Please submit questions to “All Panelists” via the chat box
  • You may enter questions at any time during the program
  • Questions will be discussed during the scheduled Q&A session
No Relevant Financial Disclosures
Scope of the Problem
National Data

Transplant trends

At a glance

113,226

people need a lifesaving organ transplant (total waiting list candidates). Of those,
73,927 people are active waiting list candidates. Totals as of today 3:31pm EST

29,844

Transplants performed this year
Total Transplants January - September 2019 as of 11/04/2019

14,361

donors
Total Donors January - September 2019 as of 11/04/2019

*Active candidates are currently suitable for transplantation and eligible to receive organ offers.
National Trends

Figure KI 18. Percentage of adults who underwent deceased donor kidney transplant within 5 years of listing in 2011 by DSA. Candidates listed concurrently in a single DSA are counted once in that DSA, from the time of earliest listing to the time of latest removal; candidates listed in multiple DSAs are counted separately per DSA.

National Trends

Figure KI 23. Pretransplant mortality rates among adults waitlisted for kidney transplant in 2016, by DSA. Mortality rates are computed as the number of deaths per 100 patient-years of waiting in the given year. Patients censored at waitlist removal. Individual listings are counted separately. Rates with less than 10 patient-years of exposure are not shown.

Figure KI 48. Total kidney transplants. All kidney transplant recipients, including adult and pediatric, retransplant, and multi-organ recipients.
Historical Background
Kidney Allocation

December 23, 1954 – first kidney transplant at Brigham & Women’s
Pre-1968 – Deceased donor kidneys allocated locally
1968 – Southeast Organ Procurement Foundation
1977 – SEOPF instituted United Network of Organ Sharing (computer-based matching)
1984 – UNOS separated from SEOPF; Congress passed the National Organ Transplant Act (Organ Procurement and Transplantation Network [regulatory body]).
1986 – UNOS and OPTN become 1 allocation and regulatory entity.
1999 – UNET (secure internet-based database system).
2000 – OPTN Final Rule to establish “equitable allocation of deceased donor organs among potential recipients”.

OPTN FINAL Rule

Roadmap for allocation policy and specified that allocation must be:
1. Based on sound medical judgment.
2. Seek to achieve best use of donated organs.
3. Designed to avoid wasting organs, avoid futile transplants.
4. Promote patient access to transplantation.
Kidney Allocation System

Pre-KAS
1. Most allocation based on *wait time* (utility?).
   1. 20-yr old donors going to 70+ yr old recipients
2. Minority groups waited longer on wait list (justice? equity?).
3. Minority groups less likely to be referred for transplant – long periods of dialysis.
4. Regional variations in access.

Kidney Allocation System

Standard Criteria vs Extended Criteria (binary)
Life years from Transplantation – how many more years gained from kidney transplantation
Kidney Donor Risk/Profile Index
Wait time calculation (based on initiation of dialysis or GFR)
Blood group preferences (A2, A2B to B candidates)
Elimination of the payback system
Estimated Post-Transplant Survival replaced LYFT
Age mismatch ±15 years
Highly-sensitized patients (>98% PRA)

Ramifications of KAS
Highly-sensitized Patients

Figure 1. Percentage of kidneys in each kidney donor profile index (KDPI) category used for recipients with calculated panel-reactive antibody (cPRA) levels ≥ 99% compared to the representation of candidates with cPRA levels ≥ 99% on the waitlist. Waitlist percentage represents the percentage of the deceased donor waitlist comprising candidates with cPRA levels ≥ 99% on January 1 of each respective year. Calculations for column graph series are as shown for this example: [# of KDPI ≤ 20% kidneys used for cPRA ≥ 99% candidates/total # of KDPI ≤ 20% kidneys] × 100. Abbreviation: KAS, kidney allocation system.

Highly-sensitized Patients

Figure 4. Cumulative incidence of kidney graft failure stratified by (A) calculated panel reactive antibody (cPRA) level and (B) kidney donor profile index (KDPI) score.

FIGURE 1 Access to transplant score (ATS) standard deviations ($SD_w$) by quarter, 2010-March 31, 2017. The Winsorized $SD_w$ of ATS quantifies the degree of disparity in access to deceased donor transplantation among active kidney-alone waiting list candidates. High values are associated with greater disparities in access. Before the kidney allocation system (KAS), $SD_w$ ranged between 1.15 and 1.46 but fell $\approx$40% with the new (KAS), suggesting improved equity.
Access to DDKT post-KAS

**Figure 3** Comparison of factor-specific standard deviations ($SD_w$), January 1-March 31, 2017. For the most recent period, DSA of listing had the strongest association with disparities in access to deceased donor kidney transplantation, as reflected by the highest $SD_w$ of 0.57. Candidate CPRA, blood type (ABO), and diagnosis had the next highest $SD_w$ values. $SD_w$ was < 0.10 for all demographic and socioeconomic factors. CPRA, calculated panel-reactive antibody; DSA, donor service area.


### Table 4. Perioperative Costs Compared Pre- and Post-Kidney Allocation System

<table>
<thead>
<tr>
<th>Cost</th>
<th>Pre-KAS (n = 21,450), mean ± SD</th>
<th>Post-KAS (n = 16,566), mean ± SD</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total costs, $</strong></td>
<td>97,244 ± 2,561</td>
<td>106,503 ± 2,359</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Total direct costs, $</strong></td>
<td>69,731 ± 1,751</td>
<td>76,334 ± 1,759</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Direct costs index</strong></td>
<td>1.00 ± 0.02</td>
<td>1.10 ± 0.03</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Category, $</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Organ procurement</td>
<td>52,883 ± 1,273</td>
<td>57,446 ± 1,565</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Surgical</td>
<td>3,914 ± 155</td>
<td>4,372 ± 118</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pharmacy</td>
<td>5,301 ± 311</td>
<td>5,954 ± 250</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Accommodations</td>
<td>4,330 ± 189</td>
<td>4,708 ± 180</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Laboratory</td>
<td>1,152 ± 44</td>
<td>1,214 ± 44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Transfusion</td>
<td>1,083 ± 143</td>
<td>1,268 ± 156</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Medical/surgical supplies</td>
<td>1,266 ± 62</td>
<td>1,329 ± 74</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Imaging</td>
<td>275 ± 15</td>
<td>286 ± 10</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

KAS, kidney allocation system.
Cost

Longer CIT associated with increased rate of DGF (OR, 1.41) and increased LOS (OR, 1.04).

Recipients who developed DGF had longer LOS (OR, 1.71).

After adjusting for LOS, an increased LOS resulted in an increase in TRC by $3422 per additional day.

Effect of CIT on TRC is partially mediated through LOS.
FIGURE 1. Schematic representation of the putative direct and indirect association of kidney allocation system (KAS), cold ischemia time (CIT), delayed graft function (DGF)/slow graft function (SGF), length of stay (LOS), and their impact on transplant-related cost. The arrows demonstrate points of statistical association and build a model demonstrating association of increased transplant-related cost and increased in CIT associated with the revised KAS. SRTR, Scientific Registry of Transplant Recipients; UMN, University of Minnesota.
Kidney Discard

Figure 2: Relationship between the kidney discard rate and the Kidney Donor Profile Index (KDPI). As the KDPI increases, the percentage of recovered kidneys that are not transplanted (i.e., the discard rate) rises precipitously. Analyses are based on kidneys recovered for transplantation between December 4, 2014, and May 31, 2016, and for which KDPI was correctly calculated in DonorNet.

Kidney Discard

1. 3% kidneys KDPI 0-20%; 60% KDPI >85%.
2. System level factors: cold ischemia time, increasing refusal number, nighttime offer (11.00 p.m. to 5.00 a.m.), absence of kidney photograph on DonorNet, and neither kidney placed at time of offer.
3. **18-19%** procured kidneys are discarded.
Kidney Discard

Figure 2 | The frequency, type (single, unilateral, or bilateral), and proportion of US deceased donor kidney discards stratified by year of procurement (n = 36,700), 2000 to 2015.

Kidney Discard


Figure 4 | US organ quality (Kidney Donor Profile Index [KDPI]) of deceased donor kidney discards stratified by discard type (*n* = 36,700), 2000 to 2015.
Kidney Discard

Figure 5 | Kidney Donor Risk Index (KDRI) overlap of transplanted and discarded kidneys recovered from 2000 to 2015.

## Kidney Discard

### Table 2: Common causes of kidney discard by discard quality and type of organs procured in the US between 2000 and 2015 (N = 36,700)

<table>
<thead>
<tr>
<th>Discard type</th>
<th>N (row %)</th>
<th>Extended ischemia</th>
<th>Organ damage</th>
<th>Anatomical abnormality</th>
<th>Poor function</th>
<th>Donor history</th>
<th>No recipient located</th>
<th>Other</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single</td>
<td>1.9</td>
<td>6.5</td>
<td>9.6</td>
<td>10.0</td>
<td>7.2</td>
<td>29.0</td>
<td>18.0</td>
<td>18.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bilateral</td>
<td>1.8</td>
<td>1.6</td>
<td>5.2</td>
<td>9.8</td>
<td>8.8</td>
<td>43.7</td>
<td>15.1</td>
<td>14.1</td>
<td></td>
</tr>
<tr>
<td>Unilateral</td>
<td>5.0</td>
<td>10.2</td>
<td>12.4</td>
<td>9.2</td>
<td>6.5</td>
<td>20.6</td>
<td>12.4</td>
<td>23.8</td>
<td></td>
</tr>
</tbody>
</table>

### Organ quality

- **Median KDRI (IQR):**
  - Single: 1.59 (0.61), 1.29 (0.71), 1.66 (0.75), 1.73 (0.73), 1.65 (0.74), 1.90 (0.72), 1.83 (0.74), 1.64 (0.75), <0.001
  - Bilateral: 76.5 (32.5), 57 (54), 80 (37), 84 (31), 80 (35), 89 (22), 87 (25), 79 (36), <0.001
  - Unilateral: 1.10 (0.70), 1.0 (0.70), 1.10 (0.70), 1.40 (1.34), 1.10 (0.80), 1.30 (0.90), 1.20 (0.98), 1.10 (0.90), <0.001

- **Median terminal sCr (mg/dl) (IQR):**
  - Biopsy performed: 2.3, 1.8, 4.9, 9.3, 5.8, 46.4, 15.8, 13.9, <0.001

### Discarded locally

- **Yes:** 2.0, 3.8, 7.2, 9.0, 9.8, 37.2, 17.2, 14.0, <0.001
- **No:** 4.4, 3.5, 6.4, 11.5, 5.0, 43.8, 3.7, 21.7
- **Unknown:** 2.0, 3.2, 6.4, 9.8, 6.3, 34.8, 19.4, 18.2

IQR, interquartile range; KDPI, Kidney Donor Profile Index; KDRI, Kidney Donor Risk Index; sCr, serum creatinine; UNOS, United Network of Organ Sharing.

*KDPI is calculated based on a scaling factor of 1.2175005163, a median KDRI value among all deceased donor kidneys procured during 2015.*

Kidney Discard

Figure 6 | The adjusted odds ratio (aOR) of discard by United Network for Organ Sharing region, 2000 to 2015.

KDPI Criticism

1. Developed in USA

2. Any midsized Caucasian donor >63 y.o. without any known comorbidities will present with a KDPI >85%.
   1. In Europe, 32.4% of donors in 2015 were >70 y.o.; only 46.8% were <60 y.o.

3. Adequate for GFR prediction.

4. Does not provide any additive discrimination above donor age alone in terms of graft failure prediction.
High KDPI (>85%) Kidneys
Survival Benefit of High KDPI Kidney

Survival Benefit of in >60 y.o.

Figure 2 Adjusted patient survival. A. Patient survival for recipients of preemptive-high KDPI kidneys compared to 1-4 years dialysis vintage-lower KDPI kidneys; B: Patient survival for recipients of preemptive-high KDPI kidneys compared to 4-8 years dialysis vintage-lower KDPI kidneys. KDPI: Kidney donor profile index.

Survival Benefit of in >60 y.o.

FIGURE 1. Patient survival for preemptive and non-preemptive KDPI > 85% kidney transplant compared with waitlist including KDPI 0 to 85% transplantation in patients > 60 years old.

Survival Benefit of in >50 y.o.

Kidney Mate Analysis: Cold Ischemia Time

Incidence of delayed graft function among 7402 mate kidneys with Kidney Donor Profile Index ≥85%.

Kidney Mate Analysis: Cold Ischemia Time

Overall graft survival stratified by Kidney Donor Profile Index among 64,970 mate kidneys.

Kidney Mate Analysis: Cold Ischemia Time

Kaplan–Meier analysis of graft survival between mate kidneys for groups 1 (a), 2 (b), and 3 (c).

Effect of Delayed Graft Function

Figure 1 | Graft and patient survival in DGF and non-DGF cases in a paired analysis. Deceased donor kidney transplant recipients who developed delayed graft function (DGF) had inferior unadjusted graft survival and functional graft survival, particularly in the first year, when compared with recipients who received the mate kidney from the same donor but did not develop DGF. TX, transplantation.

Effect of Delayed Graft Function


Figure 2 | The relative risk of death with transplantation (with and without DGF) compared with those remaining on WL. The relative risk of death in deceased donor transplant recipients who developed delayed graft function (DGF) and who did not develop DGF (No DGF) compared with wait-listed (WL) patients. Transplant recipients in each group were compared with wait-listed patients of similar risk who had been on dialysis for equal lengths of time but who had not yet received a kidney transplant. The risk of death immediately after transplantation (TX) was higher in transplant recipients than in wait-listed patients and was highest in recipients who developed DGF. The long-term risk of death was lower with transplantation, but patients with DGF took longer to achieve an equal risk of death than did wait-listed patients.
Kidney Utilization Around the World
French Comparison

Time Frame: 2004-2014

United States: 156,089 DD kidneys; 27,987 (17.9%) discarded

France: 29,984 DD kidneys; 2,732 (9.1%, p<0.001) discarded

Kidney quality showed little change in the United States over time (mean KDRI, 1.30 in 2004 vs 1.32 in 2014); rising KDRI in France (mean KDRI, 1.37 in 2004 vs 1.74 in 2014; p< 0.001).
French Comparison

The French-based allocation model applied to the US population found that 17,435 (62%) discarded kidneys would have been transplanted in France.

Redesigned system with more aggressive organ acceptance practices would generate an additional 132,445 allograft life-years in the United States over the 10-year observation period.
French Comparison

French Comparison

German Comparison

Population: 987 adult kidney transplants at single center.
Median KDPI: 66%; higher proportion of >85% KDPI kidneys compared with US cohort (32.3% vs 9.2%).
Elderly patients (≥65 y.o.), 62% received >95% KDPI kidneys.

Patients receiving ≥99% KDPI kidneys had a 5-year death-censored graft survival (72.9%). The 5-year survival rate of patients living with a functioning graft exceeded the matched OPTN data, despite a higher proportion of elderly recipients. Multivariate analysis revealed KDPI as an independent risk factor for graft loss (hazard ratio 1.14/10%, P < 0.001).


**Figure 2**: Patient (A), graft survival (B, C) and graft function (D) by KDPI category. Median eGFR using imputation for values after graft loss (patients with graft loss; GFR = 0 mL/min/1.73 m²). eGFR was calculated using the Modification of Diet in Renal Disease formula [19].
German Comparison

**FIGURE 3:** Comparison of living with functioning graft at 5 years post-transplant: study cohort versus OPTN data.

Spanish Comparison

Time Frame: Jan 2006 to Dec 2015

KDPI accurately discriminates optimal organs from suboptimal or marginal ones.

Multivariate analysis identified the KDPI, donor age, donation after circulatory death, recipient age and gender as predictive factors of graft survival.

Figura 2 – Supervivencia del injerto por Kaplan-Meier de acuerdo con el cuartil de KDPI para receptores entre 18 y 59 años: a) censurada para muerte; b) no censurada.
Figura 3 – Supervivencia del injerto por Kaplan-Meier de acuerdo con el cuartil de KDPI para receptores mayores de 60 años: a) censurada para muerte; b) no censurada.
Research at Hartford Hospital on High KDPI Kidneys
Donor-Recipient Matching to Optimize the Utility of High KDPI Kidneys

**Objective:** To understand donor and recipient characteristics that yield a successful high KDPI DDKT.

**Study Time Period:** December 2014-July 2019

**Methods:** Multivariable regression of High KDPI recipients, stratified according to 1-year creatinine; modeling of donor and recipient characteristics predictive of a creatinine <1.7.

**Study Population:** 55 High KDPI recipients (377 DDKT; 14%)
## Donor Characteristics

<table>
<thead>
<tr>
<th>Donors</th>
</tr>
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<tbody>
<tr>
<td>N</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Male Gender (%)</td>
</tr>
<tr>
<td>African American (%)</td>
</tr>
<tr>
<td>Hypertensive (%)</td>
</tr>
<tr>
<td>Diabetic (%)</td>
</tr>
<tr>
<td>Serum Creatinine (mg/dL)</td>
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<tr>
<td>Cardiovascular Cause of Death (%)</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
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<tr>
<td>DCD (%)</td>
</tr>
<tr>
<td>Hepatitis C (%)</td>
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<td>Cold Time (hours)</td>
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<td>KDPI</td>
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*T. L. Blake-Popham et al. Unpublished Data.*
# Donor Characteristics

<table>
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<th>Condition</th>
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<tr>
<td>Glomerulosclerosis (%)</td>
<td>5.2</td>
</tr>
<tr>
<td>Presence fibrosis/atrophy (%)</td>
<td>50</td>
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<tr>
<td>Presence of arteriosclerosis (%)</td>
<td>47.2</td>
</tr>
<tr>
<td>Presence of hyalinosis (%)</td>
<td>18.1</td>
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<tr>
<td>Pump Flow</td>
<td>134</td>
</tr>
<tr>
<td>Pump Resistance</td>
<td>0.23</td>
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</table>

*T. L. Blake-Popham et al. Unpublished Data.*
## Recipient Characteristics

<table>
<thead>
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<th>Recipients</th>
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</thead>
<tbody>
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<td>N</td>
<td>55</td>
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<tr>
<td>Age</td>
<td>62.27</td>
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<tr>
<td>Male Gender (%)</td>
<td>67.2</td>
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<tr>
<td>African American (%)</td>
<td>32.7</td>
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<td>Hypertensive (%)</td>
<td>92.7</td>
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<td>Diabetic (%)</td>
<td>49</td>
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<tr>
<td>Time Listed (days)</td>
<td>1181</td>
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<tr>
<td>BMI</td>
<td>29.5</td>
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Kinetics of Kidney Function After DDKT

Cr 1.7 at 1 year

Outcomes

LOS: 6.8 days
30-day readmission rate: 43%
DGF: 54%
6-month creatinine: 1.73±0.66 (n=43)
1-year creatinine: 1.67±0.52mg/dL (n=37)

Graft survival: 92.7%
Death-censored graft survival: 96.2%
Patient survival: 96.4%

Multivariable Model Predictive of 1-year Cr 1.7

Donor characteristics suggestive of Cr >1.7 at one year:
Fibrosis on biopsy (p=0.07)

Recipient characteristics suggestive of Cr >1.7 at one year:
Younger age (p=0.075)

Recipient characteristics predictive of Cr >1.7 at one year:
Male gender (p=0.016)
African American race (p=0.039)
Conclusions

The wait list for KT continues to grow each year. Wait time for a KT is highly dependent on geography. Kidney allocation is a balance between equity, fairness, justice, and utility. A KT (of any quality) is better than HD for all age groups.
Conclusions

Discard rates in the US are exceedingly high. Utilization of kidneys is highly dependent on geography.

Kidney travel ➔ increased CIT ➔ increased LOS ➔ increased Cost

Improvements in High KDPI kidney utilization in the US must improve.

High KDPI kidney utilization requires a multifaceted evaluation that takes into account donor and recipient characteristics for an ideal match.
Thank you

Oscar K. Serrano, MD, MBA
Oscar.serrano@hhchealth.org

Do all the good you can.
By all the means you can.
In all the ways you can.
In all the places you can.
At all the times you can.
To all the people you can.
As long as ever you can.
- John Wesley
For more information:

Danielle Daley, MBA  
Executive Director  
(203) 285-1212  
danielle.daley@ipro.us

Sarah Keehner, RN, BSN, CNN  
Quality Improvement Director  
(203) 285-1214  
sarah.keehner@ipro.us

Megan Perras  
Quality Improvement Coordinator  
(203) 285-1224  
megan.perras@ipro.us

Jaya Bhargava, PhD, CPHQ  
Regional Operations Director  
(203) 285-1215  
jaya.Bhargava@ipro.us

Agata Roszkowski, LMSW  
Patient Services Director  
(203) 285-1213  
agata.rozkowski@ipro.us

Corporate Headquarters  
1979 Marcus Avenue  
Lake Success, NY 11042-1072  
http://ipro.org