Opportunities to Increase Deceased Donor Kidney Utilization

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Kidney utilization: A complex decision-making process

- Donor factors
  - Age, history, co-morbidities
  - Renal function
  - Gross morphology
  - Biopsy findings
  - Cold ischemia time: pump vs static
  - Pump parameters
- Recipient factors
- Transplant center operational factors
- Transplant program performance/regulatory factors

Increasing kidney utilization: Where are the opportunities?

Factors leading to the discard of deceased donor kidneys in the United States

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The proportion of deceased donor kidneys procured for transplant but subsequently discarded has been growing steadily in the United States, but factors contributing to the rising discard rate remain unclear. To assess the reasons for and probability of organ discard we assembled a cohort of 212,305 deceased donor kidneys recovered for transplant from 2000-2015 in the SRTR registry that included 36,700 kidneys that were discarded. 'Biopsy Findings' (38.2%) was the most commonly reported reason for discard. The median Kidney Donor Risk Index of discarded kidneys was significantly higher than transplanted organs (1.78 vs 1.12), but a large overlap in the quality of discarded and transplanted kidneys was observed. Kidneys of donors who

Kidney transplantation is the treatment of choice for patients with end-stage renal disease (ESRD).[1,2] However, the supply of kidneys available for transplantation appears to have plateaued in the United States (US). The widening gap between supply and demand for transplantable kidneys has resulted in <35% of patients being transplanted within 5 years of wait-listing, whereas only 36% of patients on dialysis survive ≥5 years.[3] Nevertheless, the number of deceased donor kidneys that are procured for transplant but

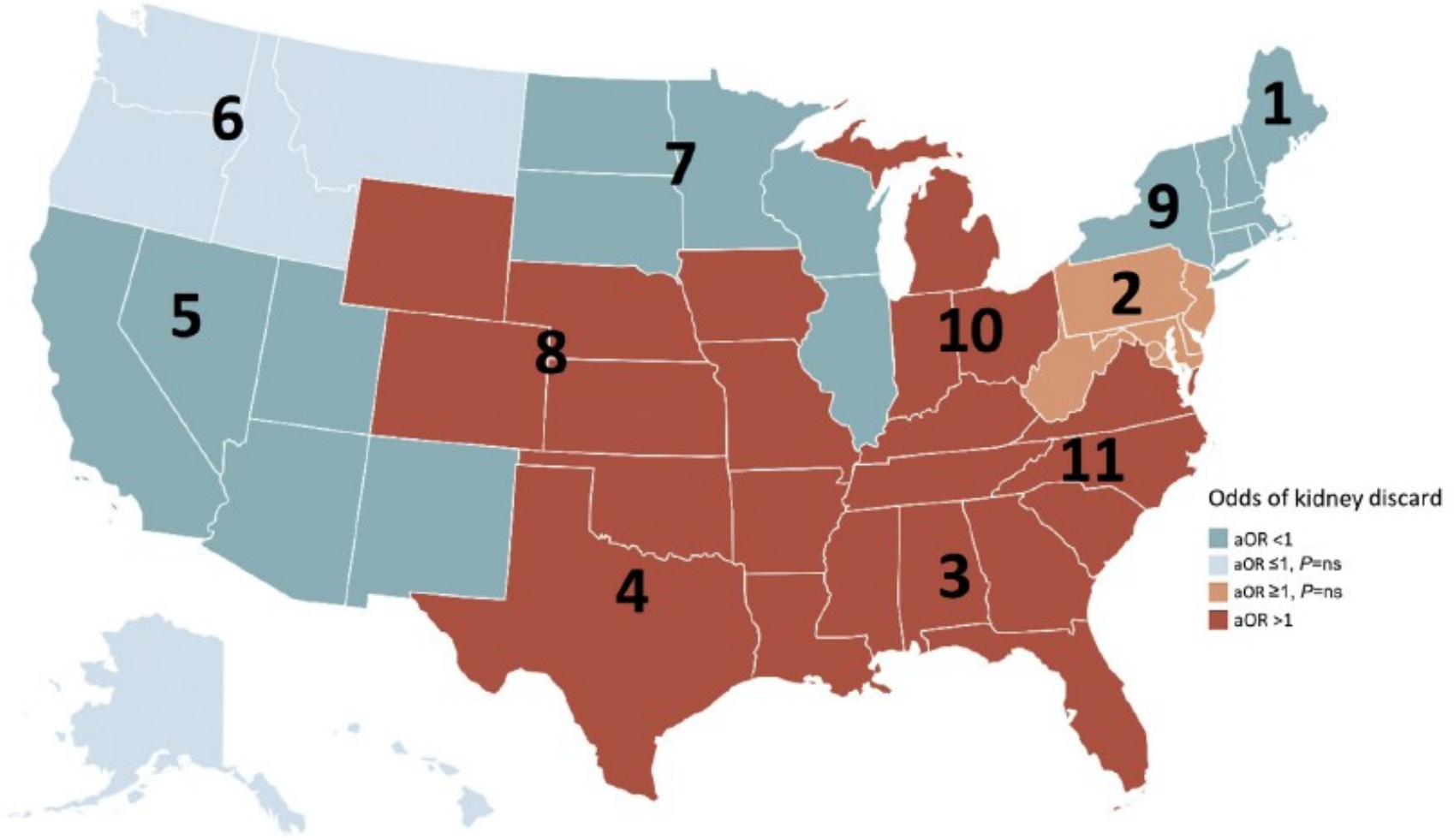
Why were these kidneys not utilized?

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

	Extended ischemia	Organ damage	Anatomical abnormality	Poor function	Donor history	Biopsy findings	No recipient located	Other	
N (row %)	912 (2.5)	1333 (3.6)	2527 (6.9)	3534 (9.6)	3019 (8.2)	14,032 (38.2)	5368 (14.6)	5975 (16.3)	*P* value
Discard type									
Single	1.9	6.5	9.6	10.0	7.2	29.0	18.0	18.0	<0.001
Bilateral	1.8	1.6	5.2	9.8	8.8	43.7	15.1	14.1	
Unilateral	5.0	10.2	12.4	9.2	6.5	20.6	12.4	23.8	
Organ quality									
Median KDRI (IQR)	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
Median KDPI (IQR)[a]	76.5 (32.5)	57 (54)	80 (37)	84 (31)	80 (35)	89 (22)	87 (25)	79 (36)	<0.001
Median terminal sCr (mg/dl) (IQR)	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
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	

Mohan et al,. Kidney International 2018

Geographic variation in utilization of kidneys: National experience 2000 - 2015



Mohan et al,. Kidney International 2018

Are many potentially transplantable kidneys not being utilized?

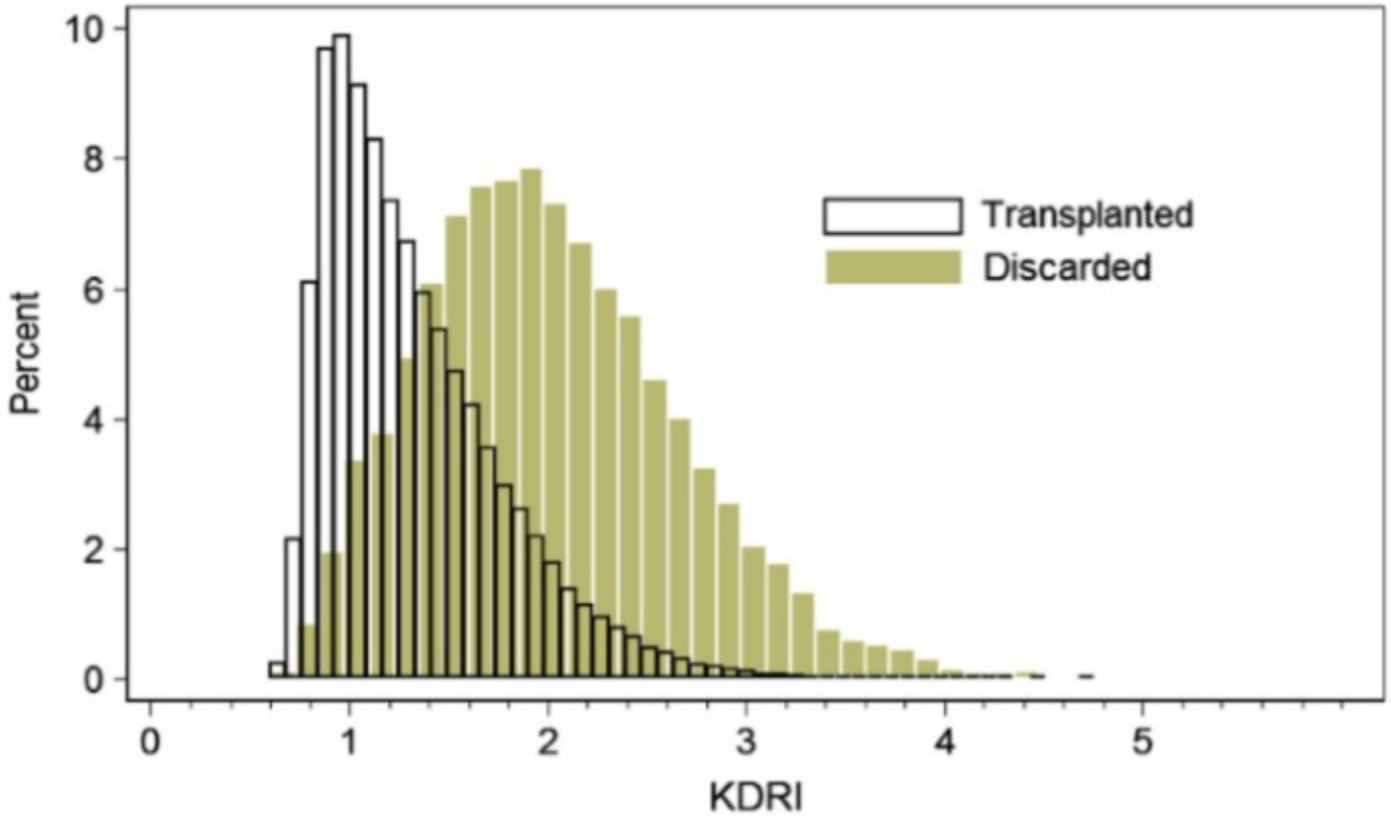


Figure 5 | Kidney Donor Risk Index (KDRI) overlap of transplanted and discarded kidneys recovered from 2000 to 2015.

Mohan et al,. Kidney International 2018

Major Variation across Local Transplant Centers in Probability of Kidney Transplant for Wait-Listed Patients

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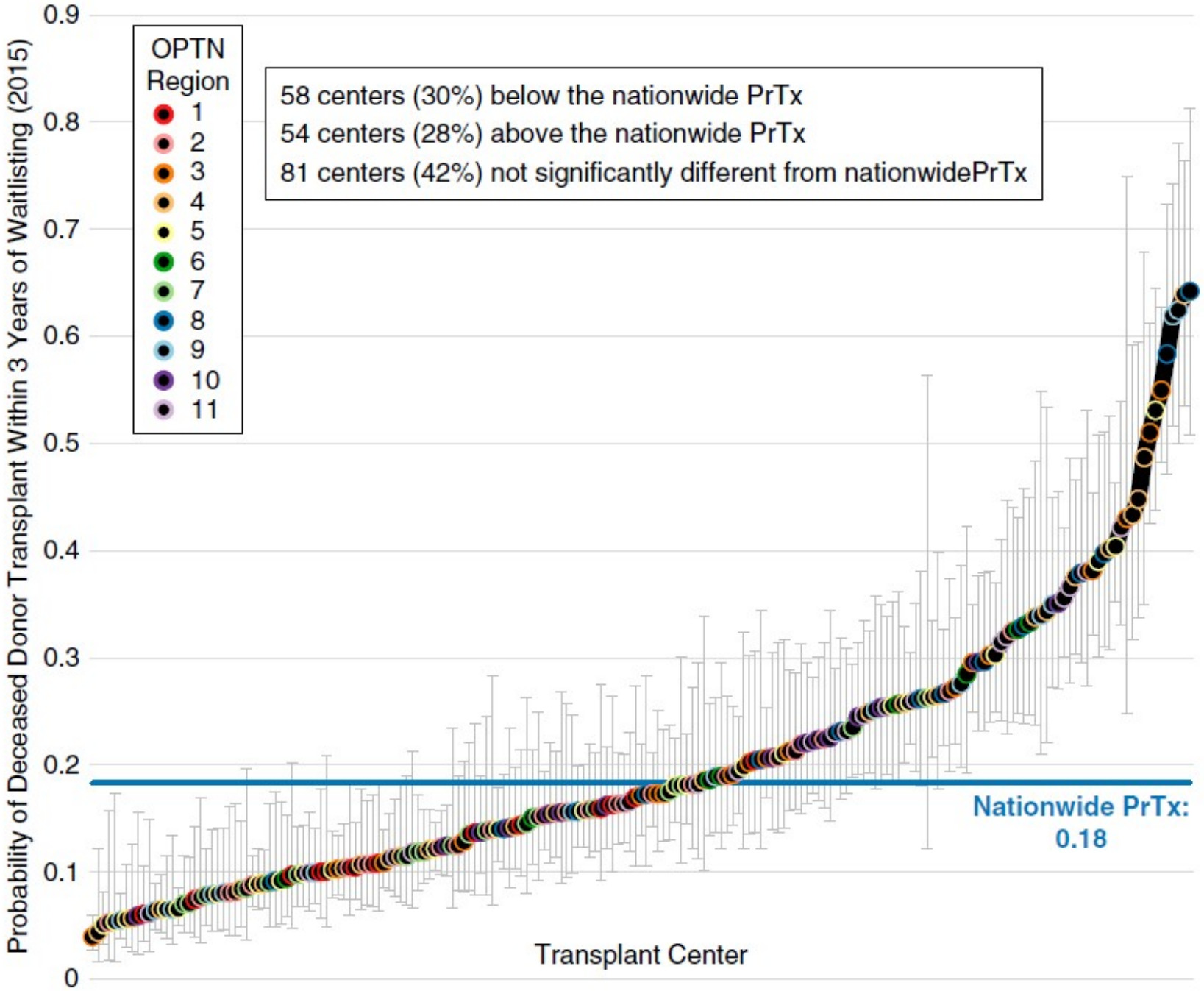
Due to the number of contributing authors, the affiliations are listed at the end of this article.

ABSTRACT

Background Geographic disparities in access to deceased donor kidney transplantation persist in the United States under the Kidney Allocation System (KAS) introduced in 2014, and the effect of transplant center practices on the probability of transplantation for wait-listed patients remains unclear.

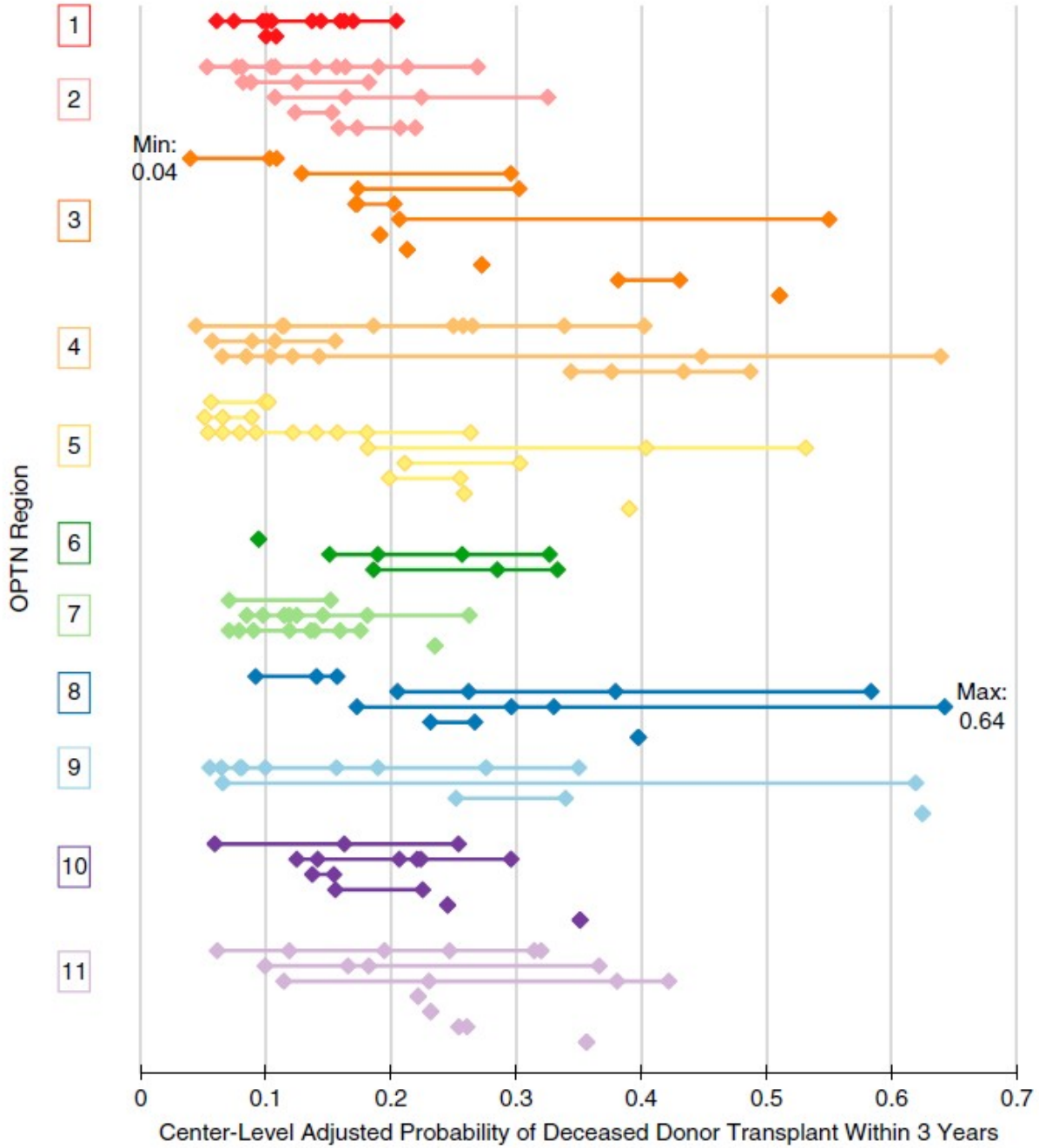
Methods To compare probability of transplantation across centers nationally and within donation service areas (DSAs), we conducted a registry study that included all United States incident adult kidney transplant

King, et al., JASN 2020



National variation in center transplant rates

King, et al., JASN 2020



Variation in center transplant rates within UNOS Regions and OPOs

King, et al., JASN 2020

Opportunities to increase kidney utilization

- Small pediatric kidneys (peds-en-bloc)
- Donors with Acute Kidney Injury (AKI)
- Expanded Criteria (High KDPI) Donors

Small Pediatric Donors

American Journal of Transplantation 2006; 6: 1646–1652
Blackwell Munksgaard

doi: 10.1111/j.1600-6143.2006.01353.x

Recovery and Utilization of Deceased Donor Kidneys from Small Pediatric Donors

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The optimal use of kidneys from small pediatric deceased donors remains undetermined. Using data from the Scientific Registry of Transplant Recipients, 2886 small (<21 kg) pediatric donors between 1993 and 2002 were identified. Donor factors predictive of

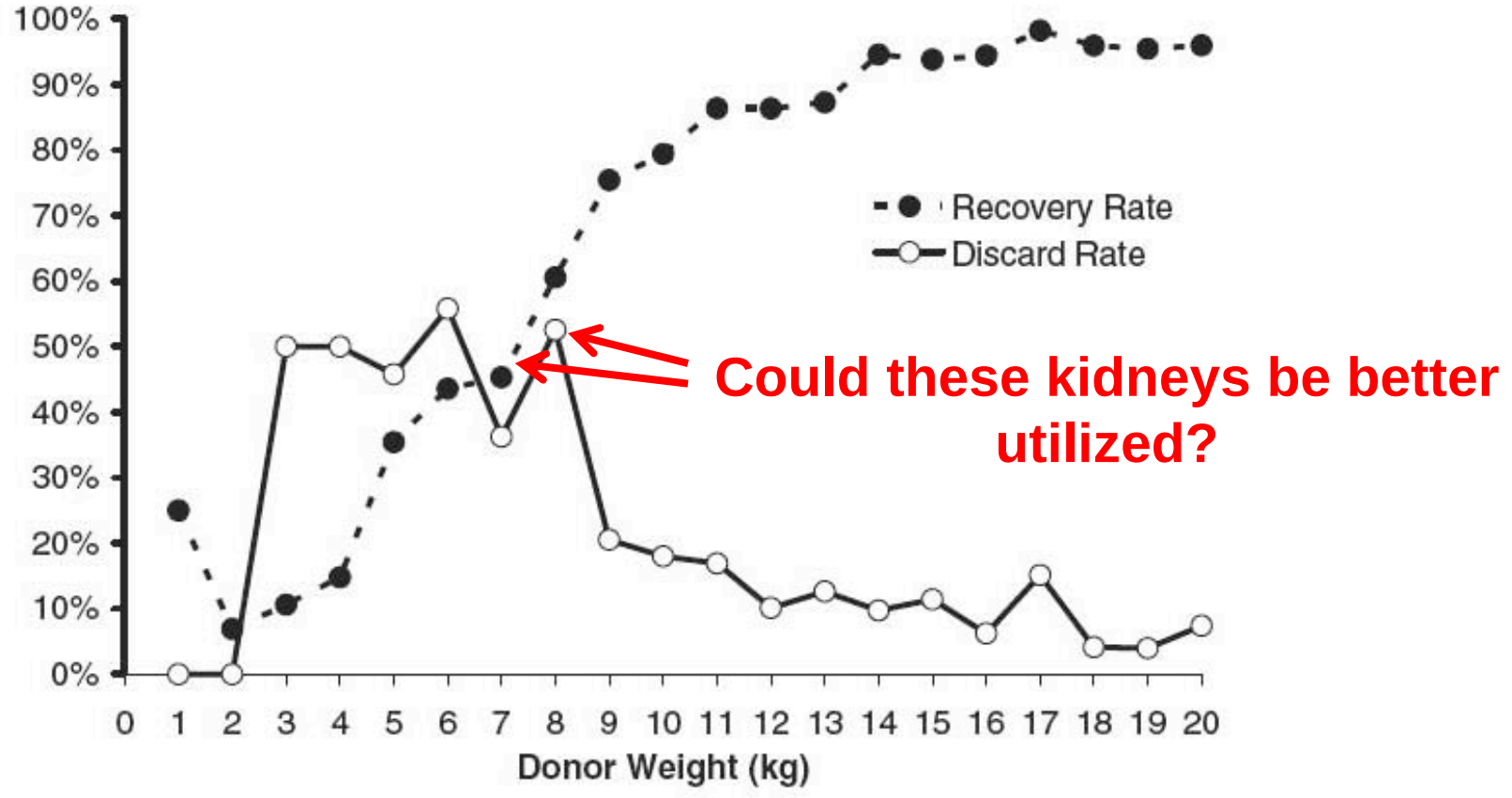
Introduction

The disparity between the number of patients with end-stage renal disease (ESRD) on the kidney transplant waiting list and the availability of deceased donor organs continues to grow. While the waiting list increased in number by more than 20% between 2000 and 2003, the number of deceased donors remained relatively stable (1). The prolonged waiting time for kidney transplantation and associated longer periods on dialysis have been associated with significant morbidity and mortality (2). While attempts have been made to maximize the donor pool, including the use of expanded criteria donors (3), donation following cardiac death and transplantation of both kidneys from an expanded criteria donor to one recipient (4–6), the optimal use of small pediatric donors has been less clear.

There has been reluctance to transplant small pediatric deceased donor kidneys into adults for several reasons

Pelletier, et al. Am J Transplant 2006

Kidneys from very small donors:
Few recovered, many discarded, few transplanted



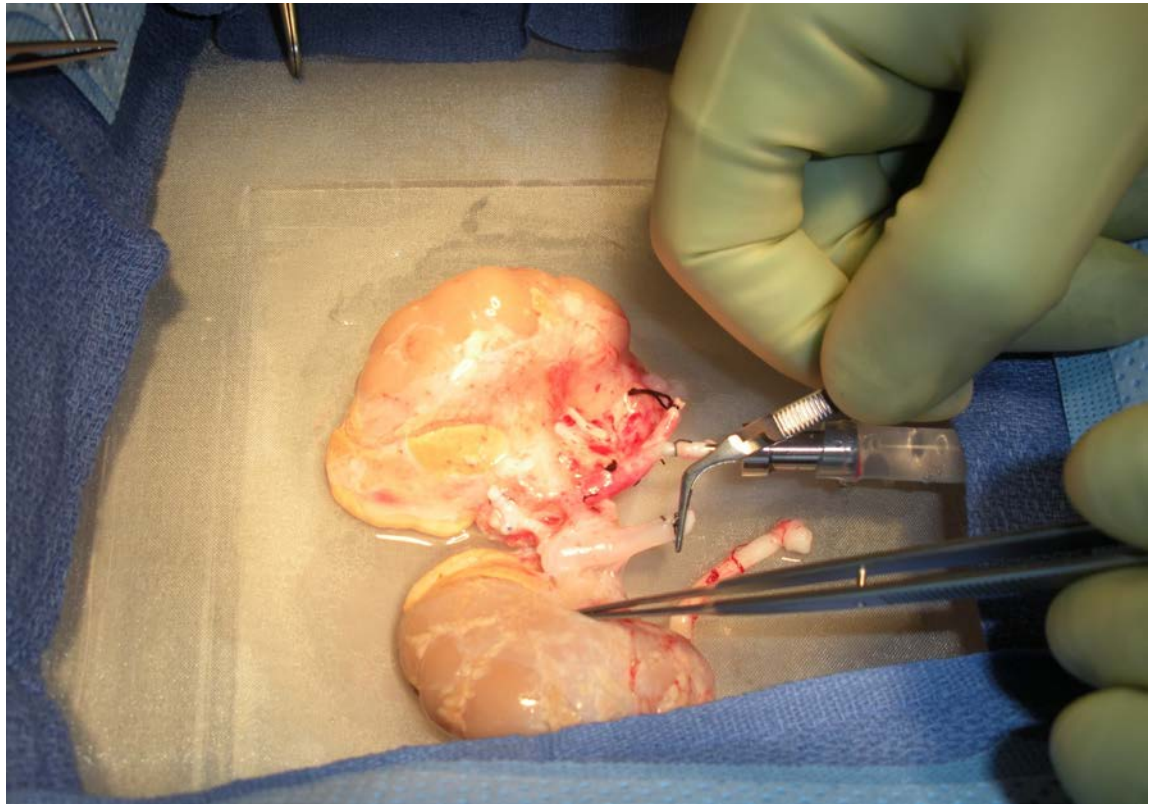
Pelletier, et al. Am J Transplant 2006

Hypothermic Pulsatile Perfusion of Small Pediatric en Bloc Kidneys: Technical Aspects and Outcomes

We read with interest the case report by Zendejas et al. (*1*) on hypothermic pulsatile perfusion (PP) of a pediatric en

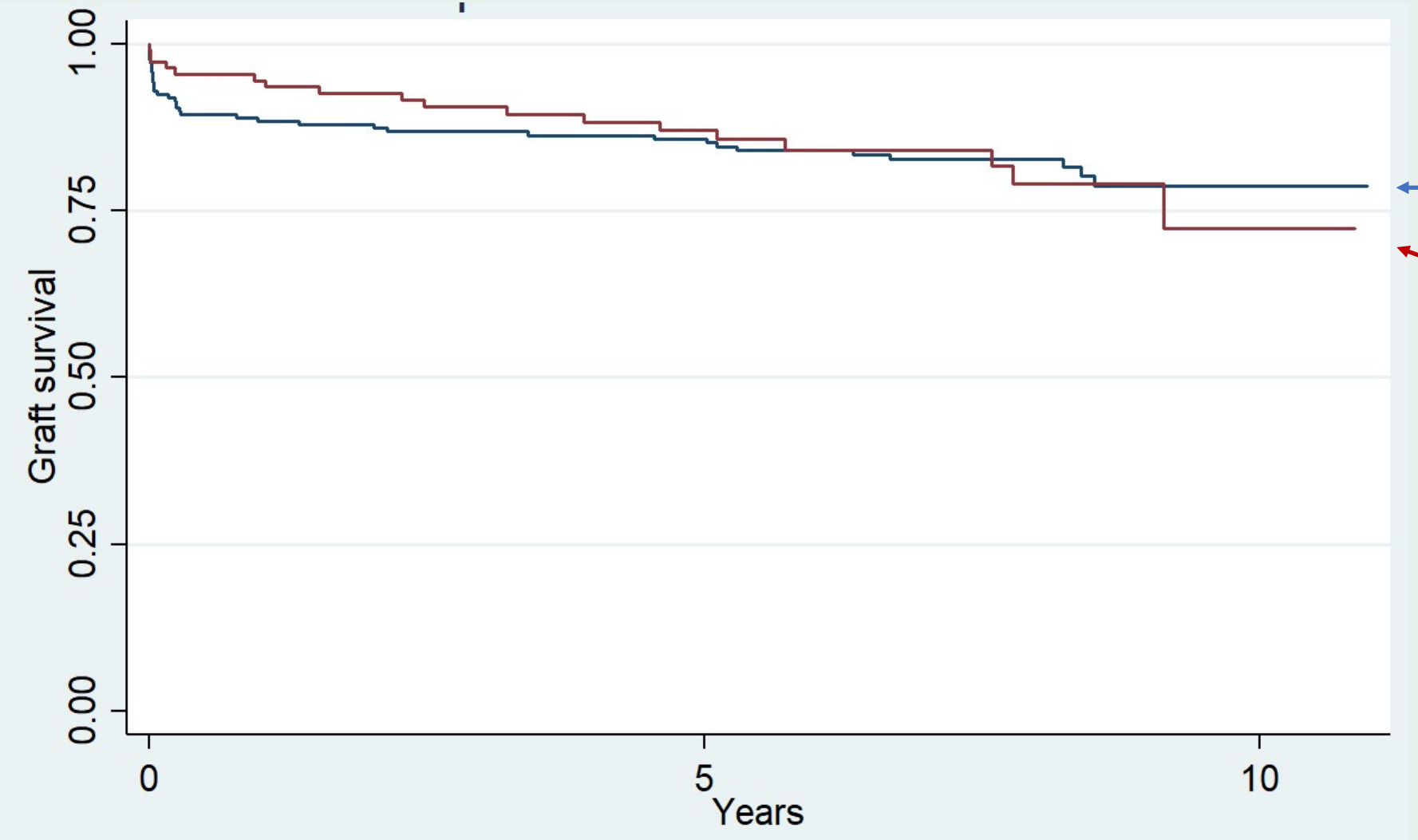
position. Such acute gravity-related effects are not observed with kidneys from larger donors.

sate at least partially for any potential graft rewarming during the more extensive backtable procedures required by en



Troppmann et. al, Transplantation 2009

Excellent long term graft survival of kidneys from small pediatric donors



Donor <10kg: n=235

Donor >10kg: n=92

UC Davis DD transplants

- **2010-2020**
- **n = 327 recipients**
- **Pediatric donors <20kg (range 1.9 – 20kg)**

BRIEF COMMUNICATION

AJT

Pediatric en bloc kidney transplantation from very small (≤10 kg) donation after circulatory death (versus brain death) donors: Single-center matched-pair analysis of 130 transplants

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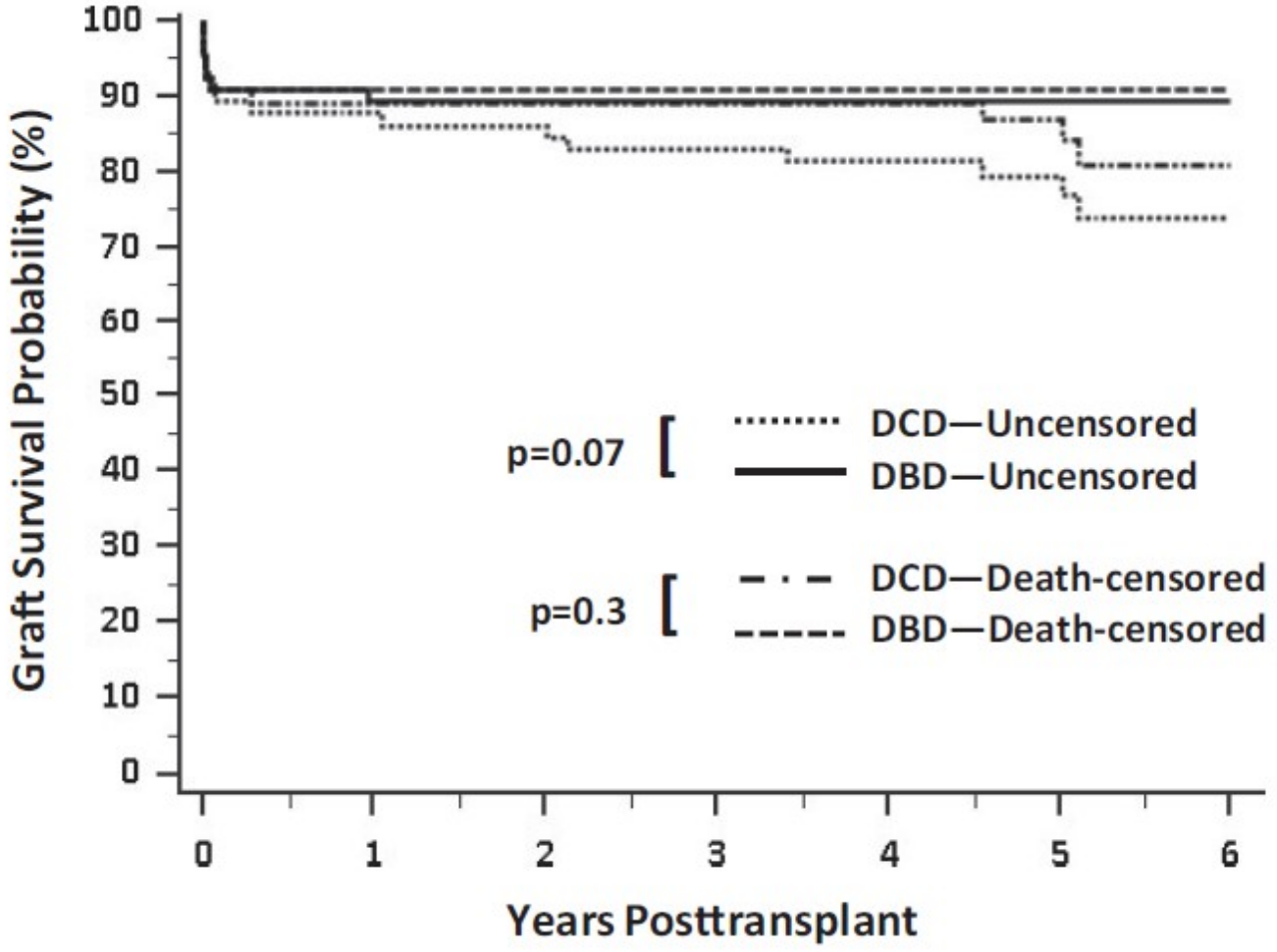
En bloc kidney transplants (EBK) from very small pediatric donation after circulatory death (DCD) donors are infrequent because of the perception that DCD adversely impacts outcomes. We retrospectively studied 130 EBKs from donors ≤10 kg (65 consecutive DCD vs 65 donation after brain death [DBD] transplants; pair-matched for donor weight and terminal creatinine, and for preservation time). For DCD vs DBD, median donor weight was 5.0 vs 5.0 kg; median recipient age was 57 vs 48 years (P = .006). Graft losses from thrombosis (DCD, 5%; DBD, 7%) or primary nonfunction (DCD, 3%; DBD, 0%) were similar in both groups (P = .7). Delayed graft function rate

Troppmann, et al., Am J Transplant 2018

No difference in DCD vs DBD small pediatric kidney graft survival



Troppmann et. al, Am J Transplant 2018

Short- and Long-term Outcomes of Kidney Transplants From Very Small (≤15 kg) Pediatric Donors With Acute Kidney Injury

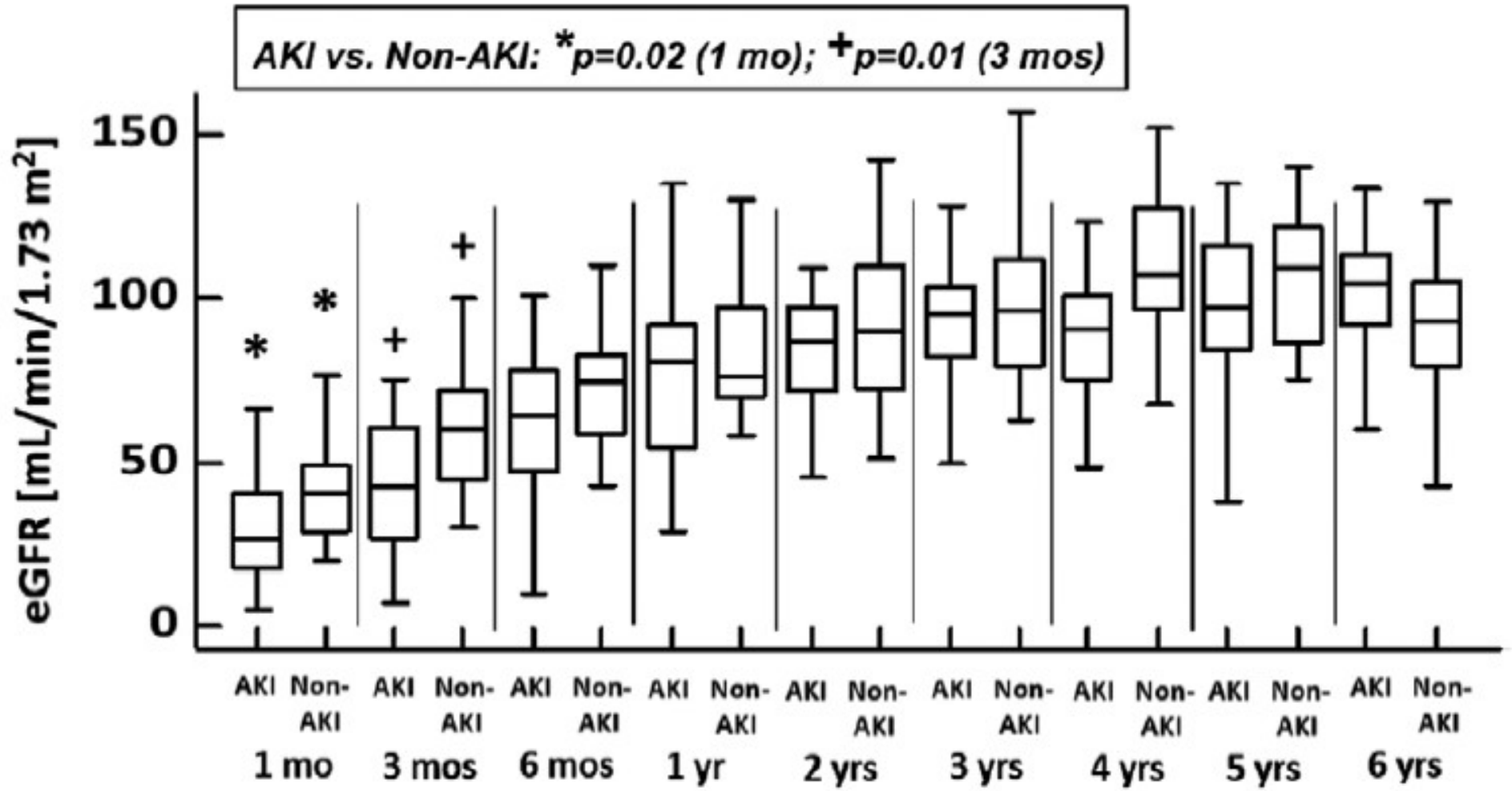
Christoph Troppmann, MD,[1] Chandrasekar Santhanakrishnan, MD,[1] Ghaneh Fananapazir, MD,[2] Junichiro Sageshima, MD,[1] Kathrin M. Troppmann, MD,[1] and Richard V. Perez, MD[1]

Background. Kidneys from small deceased pediatric donors with acute kidney injury (AKI) are commonly discarded owing to transplant centers' concerns regarding potentially inferior short- and long-term posttransplant outcomes. **Methods.** We retrospectively analyzed our center's en bloc kidney transplants performed from November 2007 to January 2015 from donors ≤15 kg into adult recipients (≥18 y). We pair-matched grafts from 27 consecutive donors with AKI versus 27 without AKI for donor weight, donation after circulatory death status, and preservation time. **Results.** For AKI versus non-AKI donors, median weight was 7.5 versus 7.1 kg; terminal creatinine was 1.7 (range, 1.1–3.3) versus 0.3 mg/dL (0.1–0.9). Early graft loss rate from thrombosis or primary nonfunction was 11% for both groups. Delayed graft function rate was higher for AKI (52%) versus non-AKI (15%) grafts ($P = 0.004$). Median estimated glomerular filtration rate was lower for AKI recipients only at 1 and 3 months ($P < 0.03$). Graft survival (death-censored) at 8 years was 78% for AKI versus 77% for non-AKI grafts. Late proteinuria rates for AKI versus non-AKI recipients with >4 years follow-up were not significantly different. **Conclusions.** Small pediatric donor AKI impacted early posttransplant kidney graft function, but did not increase risk for early graft loss and decreased long-term function. The presently high nonutilization rates for en bloc kidney grafts from very small pediatric donors with AKI appear therefore unjustified. Based on the outcomes of the present study, we infer that the reluctance to transplant single kidneys from larger pediatric donors with AKI lacks a rational basis as well. Our findings warrant further prospective study and confirmation in larger study cohorts.

(*Transplantation* 2021;105: 430–435).

Troppmann et al., Transplantation 2021

Gradual improvement of allograft function over 3 years in kidneys from small pediatric donors with AKI



Troppmann et al., Transplantation 2021

Donors with Acute Kidney Injury

Donors with AKI: Considerations

- Donor age, history, co-morbidities
- Urine output
- Admission/nadir/terminal creatinine
- General appearance/flush quality
- Biopsy – absence of diffuse cortical necrosis and absence of chronic renal disease
- Pump parameters
- Cold ischemia time

Long-term Outcomes Following Kidney Transplantation From Donors With Acute Kidney Injury

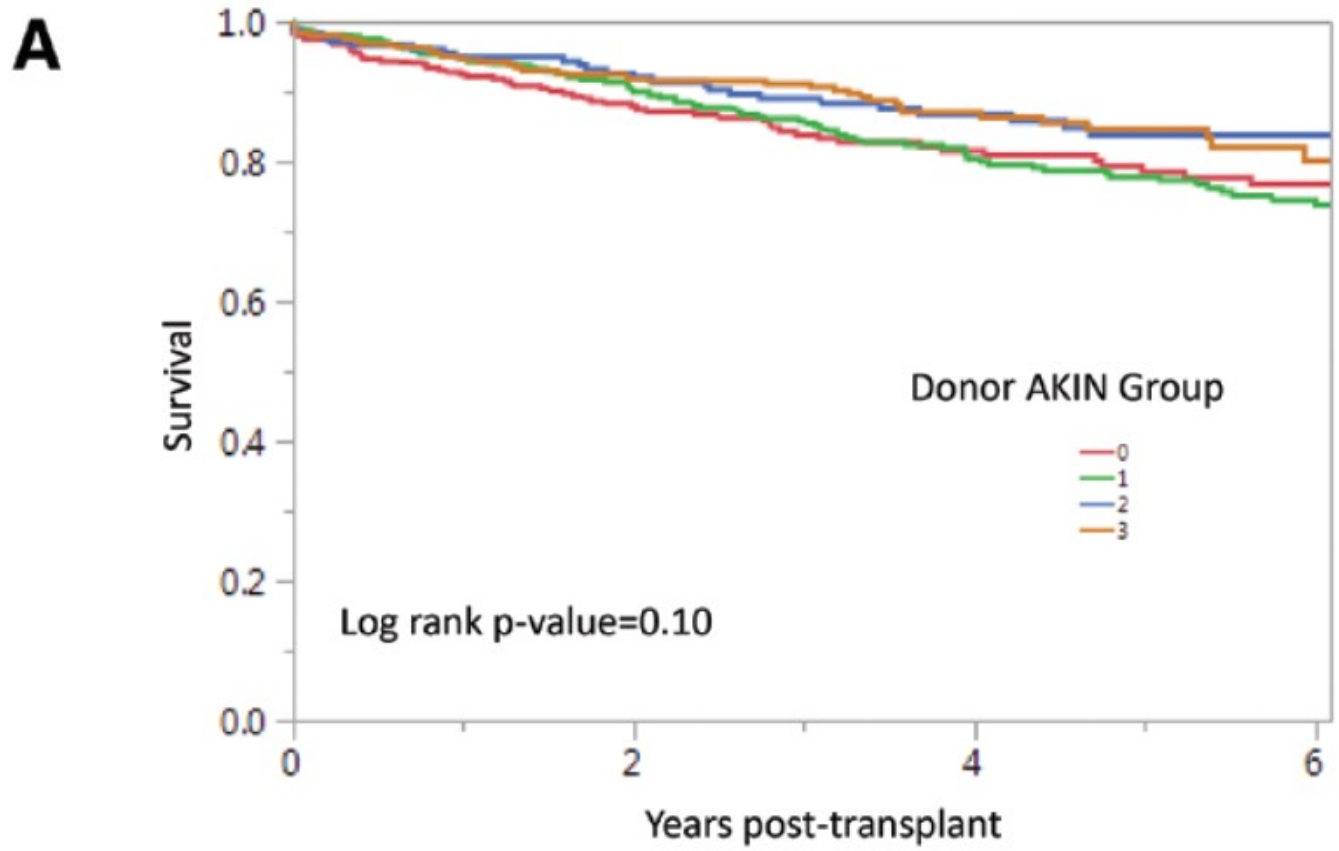
Raymond L. Heilman, MD,[1] Maxwell L. Smith, MD,[2] Byron H. Smith, PhD,[3] Anjushree Kumar, MBBS,[1] Ananth Srinivasan, MBBS,[4] Janna L. Huskey, MD,[1] Hasan A. Khamash, MD,[1] Caroline C. Jadlowiec, MD,[4] Amit K. Mathur, MD,[4] Adyr A. Moss, MD,[4] and Kunam S. Reddy, MBBS[4]

Background. Kidneys from deceased donors with acute kidney injury (AKI) are more likely to be discarded because of concerns for poor outcomes after transplantation. The aim of this study was to determine the long-term outcomes of a large cohort of patients transplanted utilizing kidneys from deceased donors with AKI. **Methods.** All patients receiving a deceased donor kidney transplant during a recent 10-year period were included. Acute Kidney Injury Network (AKIN) criteria were used to classify the donors. Donor kidneys with >10% cortical necrosis or more than mild chronic changes were discarded. The primary outcome is the combined endpoint of death or graft loss. **Results.** The cohort included 1313 kidneys from 974 donors, AKIN stage 0 (no AKI) in 319 (24.3%), stage 1 in 370 (28.2%), stage 2 in 177 (13.5), and stage 3 in 447 (34.0%). Estimated 5-year graft survival (95% confidence interval) was 78.5% (72.5-84.5), 77.8% (72.8-82.1), 83.8% (76.8-88.9), and 84.6% (79.5-88.7) for AKIN donor stage 0 to 3, respectively (log-rank $P = 0.10$). After adjusting for baseline differences, the hazard ratio (95% confidence interval) for the combined endpoint for the AKIN stage 3 group (relative to AKIN 0 group) was 0.70 (0.45-1.10). Delayed graft function occurred in 44.6% and 75.4% of AKIN 2 and 3 groups, as compared to 33.9% and 33.5% in AKIN 0 and 1 ($P < 0.001$). **Conclusion.** We conclude that transplanting selected kidneys from deceased donors with AKI with preimplantation biopsy showing <10% cortical necrosis and no more than mild chronic changes have excellent long-term graft survival.

(*Transplantation* 2019;103:e263–e272)

Heilman, et al. Transplantation 2019

Excellent graft survival after transplantation of kidneys with AKI



AKIN 0	319	232	125	84
AKIN 1	370	309	203	108
AKIN 2	177	159	99	41
AKIN 3	477	311	122	41

Heilman, et al. Transplantation 2019

Donor Characteristics, Recipient Outcomes, and Histologic Findings of Kidney Allografts With Diffuse Donor-derived Glomerular Fibrin Thrombi

Guofeng Gao, MD, PhD,[1] Ling-Xin Chen, MD,[2] Ian E. Brown, MD, PhD,[3] Angelo De Mattos, MD, MPH,[2] Richard V. Perez, MD,[4] and Kuang-Yu Jen, MD, PhD[1]

Background. Limited data are available on whether donor kidneys with diffuse glomerular fibrin thrombi (GFT) are safe to use. In this study, the clinicopathologic characteristics of allografts with diffuse donor-derived GFT were examined. **Methods.** All deceased donor kidney transplant implantation biopsies from our institution between July 2011 and February 2018 with diffuse GFT were included. A control group for comparison consisted of all cases with implantation biopsies obtained during the study period without diffuse GFT. Clinical data were extracted from electronic medical records for all study patients, including donor information. **Results.** Twenty-four recipients received kidneys with diffuse GFT from 16 deceased donors. All donors died from severe head trauma. On average, 79% of glomeruli contained fibrin thrombi. Nineteen cases had subsequent biopsy; all revealed resolution of GFT. Compared with the control group, kidneys with diffuse GFT had longer cold ischemia time (34 versus 27 h), were more frequently pumped using machine perfusion (100% versus 81%), and recipients experienced a higher frequency of delayed graft function (58% versus 27%). Only 2 grafts with diffuse GFT failed within the first year. Overall graft survival was similar between the diffuse GFT group and control group. **Conclusions.** Deceased donor kidneys with diffuse GFT appear to be safe to use given that nearly 92% of recipients in this cohort who received such allografts experienced good clinical outcomes. Histologically, GFT demonstrated rapid resolution following transplantation. Interestingly, diffuse GFT only occurred in donors who suffered severe head trauma in this cohort, which may be a predisposing factor.

(*Transplantation* 2019;103:1921–1927)

Gao, et al., Transplantation 2019

Excellent allograft function in kidneys with donor-derived diffuse glomerular fibrin thrombi

Recipient Outcomes

	Diffuse GFT	Control	P
N	24	907	
Delayed Graft Function (%)	34 (11)	27 (11)	0.001
30 day Serum Creat, mg/dL	1.96	2.07	0.67
1 year Serum Creat, mg/dL	1.17	1.40	0.08
Graft failure (%)	8.3	5.8	0.42

Gao, et al. Transplantation 2019

High KDPI Kidneys

Survival Benefit of Primary Deceased Donor Transplantation With High-KDPI Kidneys

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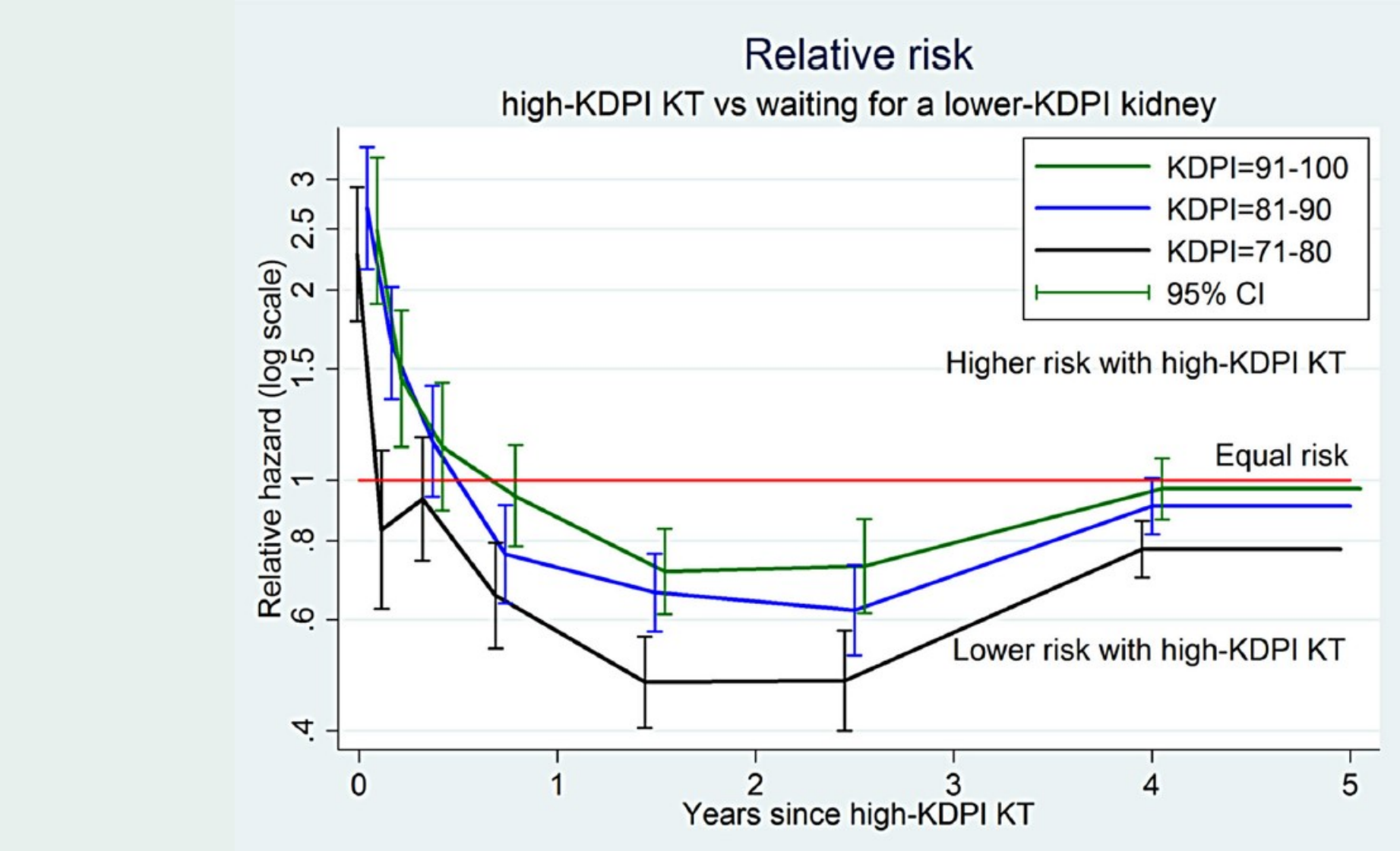
The Kidney Donor Profile Index (KDPI) has been introduced as an aid to evaluating deceased donor kidney offers, but the relative benefit of high-KDPI kidney transplantation (KT) versus the clinical alternative (remaining on the waitlist until receipt of a lower KDPI kidney) remains unknown. Using time-dependent Cox regression, we evaluated the mortality risk associated with high-KDPI KT (KDPI 71–80, 81–90 or

continuous risk score to deceased donor kidneys, based on donor and transplant characteristics collected by the Organ Procurement and Transplantation Network (OPTN) (1). As would be expected from such a regression model, estimated risk following transplantation with an expanded criteria donor (ECD) kidney was comparable to risk following transplantation with a standard criteria donor (SCD) kidney with a similar KDRI score (2). A variant of the KDRI, known as the Kidney Donor Profile Index (KDPI), is currently reported during the allocation process as a tool to aid clinicians (and presumably patients) in deciding whether or not to accept an offer of a deceased donor kidney (3). The KDPI removes transplant-related factors from the KDRI, and is normalized to a percentile score, so that (for example) risk of a kidney with a KDPI of 70 is judged to be worse than risk of 70% of kidneys recovered for transplantation in the prior calendar year.

Massie et al., Am J Transplant 2014

Survival benefit of transplantation with high KDPI kidneys



Massie et al., Am J Transplant 2014

Maximum organ utilization requires appropriate donor and recipient matching

- “One size fits all” approach can be utilized with most low-risk kidneys
- Higher risk kidneys may have an increased risk of early failure and/or risk of diminished renal function (limited reserve)
- May need to optimize donor and recipient factors
- Need to match organs and to selected recipients (age, weight, immunologic status, etc)

VIEWPOINT

Exacerbating Racial Disparities in Kidney Transplant
The Consequences of Geographic Redistribution

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Suppose for a moment that you had advanced warning a 737 jetliner with 237 people on board had a 90% probability of crashing and killing all 237 passengers and crew, along with 13 people on the ground. Would you cancel the flight?

Recently, a policy for the geographic redistribution of kidneys for transplant in the US has been approved by the Organ Procurement and Transplant Network (OPTN) board of directors. This policy was proposed upon the direction of the Secretary of the US Department of Health and Human Services and motivated by the requirement to comply with the Final Rule, which stipulates "organs and tissues ought to be distributed on the basis of objective priority criteria, and not on accidents of geography."[1] Previous studies using OPTN data concluded that geographic disparity exists across the US in access to kidney transplant, suggesting that where a person lives is associated with their access to transplant,[2] and provided the rationale for redefining geographic proximity in organ sharing from donor service areas and regions to a 250–nautical mile radius

actual disease burden. In other words, centers with large wait lists do not necessarily serve populations with a high prevalence of end-stage kidney disease. To our knowledge, no metric has been developed to determine how transplant centers meet the needs of their local population (eg, does the center wait list reflect the disease burden of the surrounding population).

An accurate measure of end-stage disease burden is critical not only for defining transplant rates and therefore ensuring those with the greatest need have the greatest access, but also for understanding organ supply for those deceased and living. It is not surprising that the population disease burden driving the need for kidney transplant is also the same population from which organ procurement organizations attempt to identify suitable deceased donors and transplant centers rely on for living donors. Multiple studies have demonstrated that kidney donation rates for living and deceased donors are decreased in areas with a high burden of end-stage kidney disease, suggesting that areas with the greatest

Hanaway, et al., JAMA Surgery; August 2020

What can we do to increase organ utilization?

- Modify current transplant program performance metrics to optimize utilization and innovation
- Adopt best practices to optimize OPO performance
- Improve allocation efficiency to minimize CIT
- Facilitate ability of transplant centers to identify appropriate patients for higher risk kidneys
- Promote more widespread utilization of hypothermic machine perfusion for higher risk kidneys