Received: 12 April 2021 | Revised: 11 November 2021 | Accepted: 2 December 2021
DOI: 10.1111/ajt.16920

ORIGINAL ARTICLE

AJT

Trends in the procurement and discard of kidneys from deceased donors with acute kidney injury

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Funding information
National Center for Advancing Translational Sciences, Grant/Award Number: UL1TR002538 and KL2TR002539; Shire; CareDx; National Heart, Lung, and Blood Institute; National Institutes of Health; National Institute of Diabetes and Digestive and Kidney Diseases; Merck; Gilead; AbbVie; University of Pennsylvania

Kidney allocation trends from deceased donors with acute kidney injury (AKI) have not been characterized since initial Kidney Donor Profile Index reporting in 2012 and its use under the revised Kidney Allocation System (KAS) in 2014. We conducted a retrospective analysis of US registry data to characterize kidney procurement and discard trends in deceased donors with AKI, defined by ≥50% or ≥0.3 mg/dl (≥4.0 mg/dl or ≥200% for stage 3) increase in terminal serum creatinine from admission. From 2010 to 2020, 172 410 kidneys were procured from 93 341 deceased donors 16 years or older; 34 984 kidneys were discarded (17 559 from AKI donors). The proportion of stage 3 AKI donors doubled from 6% (412/6841) in 2010 to 12% (1365/11493) in 2020. Procurement of stage 3 AKI kidneys increased from 51% (423/824) to 80% (2183/2730). While discard of stage 3 AKI kidneys increased from 41% (175/423) in 2010 to 44% (960/2183) in 2020, this increase was not statistically significant in interrupted time-series analysis following KAS implementation (slope difference −0.41 [−3.22, 2.4], and level change 3.09 [−6.4, 12.6]). In conclusion, the absolute number of stage 3 AKI kidneys transplanted has increased. Ongoing high discard rates of these kidneys suggest opportunities for improved utilization.

KEYWORDS
clinical research/practice, donors and donation: deceased, kidney failure/injury, kidney transplantation/nephrology, organ procurement and allocation, translational research/science

Abbreviations: AKI, acute kidney injury; BMI, body mass index; CI, confidence interval; CVA, cerebrovascular; DCD, donation after cardiac determination of death; ECD, expanded criteria donor; HCV, hepatitis C virus; HRSA, Health Resources and Services Administration; ITS, interrupted time series; KAS, Kidney Allocation System; KDIGO, Kidney Disease: Improving Global Outcomes; KDPI, Kidney Donor Profile Index; KDRI, kidney donor risk index; OPO, organ procurement organization; OPTN, Organ Procurement and Transplantation; SCD, standard criteria donor; SCr, serum creatinine; STAR, Standard Transplant Analysis and Research; UNOS, United Network for Organ Sharing.

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1 | INTRODUCTION

The US kidney transplantation system has evolved significantly within the past decade to improve allocation policies and address the growing kidney transplant waitlist. As of October 2020, the kidney transplant waitlist included 99 530 patients.[1] On March 26, 2012, the Kidney Donor Profile Index (KDPI) was first introduced as a decision aid to transplant hospitals[2] and later implemented on December 4, 2014, as part of the Kidney Allocation System (KAS).[3] KDPI is a continuous scale based on ten donor characteristics that improved upon the dichotomous standard/expanded criteria donor (SCD/ECD) classification and includes donor height, weight, terminal serum creatinine (SCr), cause of death, history of diabetes, history of hypertension, hepatitis C virus (HCV)-infection, race/ethnicity, and donation after cardiac versus brain death status.[3] Despite the move from a dichotomous measure to a continuous, surrogate measure of kidney quality, serious concerns persist that use of the KDPI has yielded unintended consequences in part due to its reliance on cross-sectional terminal kidney function data and inherent inability to account for fluctuations in deceased donor SCr prior to procurement.

Since KAS implementation, the overall deceased donor kidney discard rate has increased to approximately 20%.[4] Further subgroup analyses showed that the discard rate of high KDPI kidneys previously considered SCD rose from 46.2% to 50.7% after KDPI implementation.[5,6] This trend has been characterized by Bae et al. as the "labeling effect"[5] where high KDPI kidneys may be difficult to convince patients and providers to accept despite comparable graft survival[7] and better survival than remaining on the waitlist for a better kidney offer.[8]

Another group of kidneys that may have been impacted by the KDPI label is kidneys from deceased donors with acute kidney injury (AKI). The KDPI calculation uses the terminal SCr measurement at the time of organ procurement—a practice that fails to distinguish between transient SCr increases in deceased donors with AKI from those with preexisting chronic kidney disease.[9] Although several studies[10–14] have demonstrated good outcomes for recipients of kidneys from deceased donors with AKI, deceased donor AKI has been shown to be a strong predictor of discard for kidneys procured by five organ procurement organization (OPOs) from 2010 to 2013.[15] Nationally, 27% (4757/17 468) of kidneys procured from deceased donors with AKI were discarded from 2010 to 2013.[11] We undertook this study to characterize temporal trends in the allocation of kidneys from deceased donors with AKI in the setting of KDPI introduction and KAS implementation.

2 | METHODS

2.1 | Data source and study cohort

We used 2010–2020 DonorNet data from the Organ Procurement and Transplantation (OPTN) system. OPTN registers deceased donors and communicates organ offers to transplant hospitals with OPOs. The OPTN system includes data submitted by OPTN members on all donors, wait-listed candidates, and transplant recipients in the US. The Health Resources and Services Administration (HRSA) of the US Department of Health and Human Services provides oversight to the activities of the OPTN contractor, the United Network for Organ Sharing (UNOS). Our initial study cohort consisted of a total of 103 123 deceased donors who had at least one solid organ procured for the purpose of transplantation between January 1, 2010 and December 31, 2020 (Figure 1).

From the available 103 123 deceased donors in the OPTN registry procured during this timeframe with valid SCr values (between 0.01 and 40 mg/dl), admission dates, and aortic cross-clamp dates, we excluded donors with less than two SCr measurements between admission date and clamp date (n = 1378). Donors younger than 16 years (n = 7251) or with both kidneys transplanted in the same recipient (n = 1153) were also excluded. This provided a final cohort of 93 341 deceased donors.

DonorNet provides encrypted UNOS donor identification numbers which were linked to the UNOS Standard Transplant Analysis and Research (STAR) files to link donors with their corresponding kidney recipients and OPTN-defined recipient outcomes. Serial SCr measurements from DonorNet have previously been validated using medical record-abstracted SCr from five OPOs.[11] KDPI was retrospectively calculated relative to all deceased kidney donors procured in 2010 in the OPTN database.[16,17]

The study was approved by HRSA and the institutional review boards at participating institutions under a waiver of consent because deidentified data were used. The clinical and research activities reported herein are consistent with the Principles of the Declaration of Istanbul as outlined in the Declaration of Istanbul on Organ Trafficking and Transplant Tourism. We adhered to the ethical principles of the Declaration of Helsinki.

2.2 | Defining deceased-donor AKI

We used data from DonorNet to obtain additional SCr measurements, beyond terminal SCr alone, to identify AKI. DonorNet provides serial SCr measurements during the hospitalization of most donors. If multiple SCr measurements were available within the same day, we used the lowest SCr level on the date of hospital admission and the highest SCr level on the date of organ procurement. Deceased-donor AKI was defined as ≥50% increase in the terminal SCr level from admission or an absolute increase of at least 0.3 mg/dl (26.5 mmol/L). Stages of AKI were defined by KDIGO (Kidney Disease: Improving Global Outcomes) SCr criteria from admission to the terminal value as follows: stage 1 (≥0.3 mg/dl or 50% increase), stage 2 (≥100% increase), and stage 3 (≥4.0 mg/dl or ≥200% increase).[18] Definitions of AKI and stages of AKI were irrespective of urine output or initiation of dialysis as these data were not available.

2.3 | Statistical analysis

Continuous variables were reported as the median (interquartile range) or the mean (standard deviation). Differences in demographic

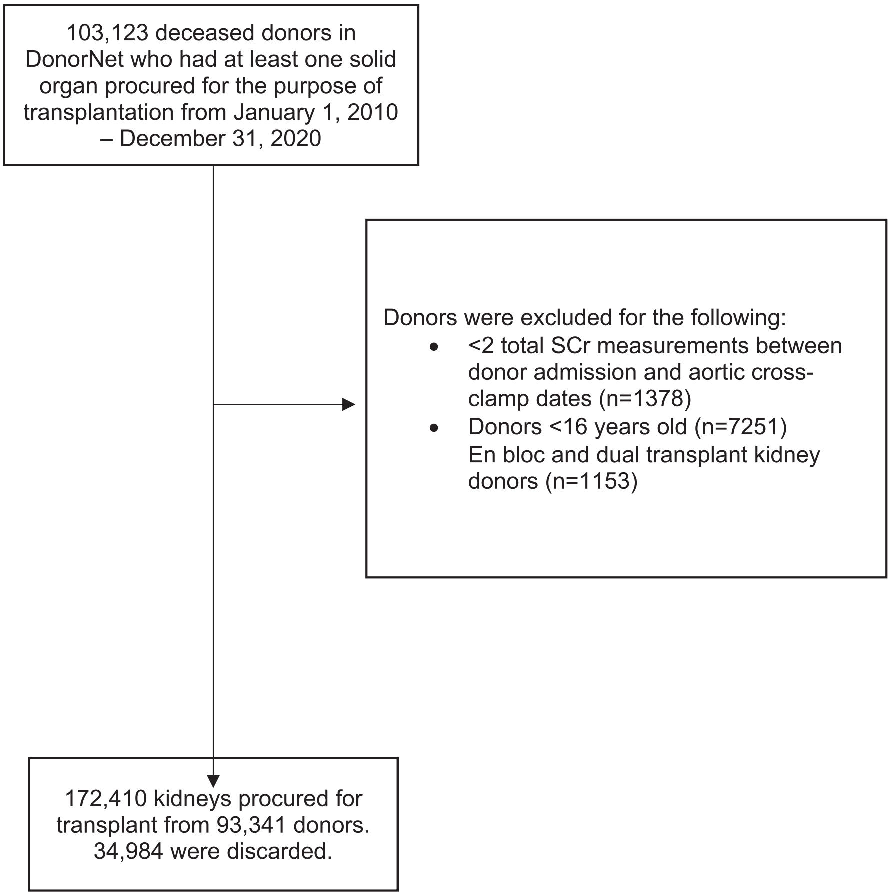

FIGURE 1 Flow chart of cohort selection. SCr, serum creatinine

characteristics, clinical characteristics, and kidney procurement characteristics were compared using Kruskal–Wallis or chi-square test for continuous and categorical variables, respectively. Differences were also reported as standardized mean differences.

We calculated the proportion of kidneys procured from deceased donors in our study cohort from January 1, 2010 to December 31, 2020. We then calculated the discard rate, defined as the percent of kidneys subsequently discarded after procurement for transplantation. We stratified trends in procurement and discard them by stages of AKI. We used interrupted time series (ITS) with linear regression modeling to quantify (1) the estimated changes in the kidney procurement rate among potential donors referred to OPOs and (2) the kidney discard rate associated with both the KDPI introduction and KAS implementation.[19] The Durbin-Watson statistic was used to test for the presence of autocorrelation. Autocorrelation and partial autocorrelation function plots were used to assess the order of autoregressive and moving average series. Plots of the rates did not reveal an effect of seasonality. Therefore, the models did not include seasonal adjustment. Final models included an error structure corresponding to an autoregression model of order 1. ITS analyses were adjusted for donor characteristics used in the KDPI calculation: Black race, hypertension, diabetes, cause of death, donation after cardiac death status, HCV antibody seropositivity status, average age, and body mass index (BMI). The following metrics were presented from the ITS Analyses: slope, slope differences, and level changes. We calculated the slopes in procurement and discard rates using pre and post KDPI periods (pre-KDPI from 2010 Q1 to 2012 Q1; post-KDPI 2012 Q2 to 2014 Q4) or pre- and post-KAS introduction periods (pre-KAS from 2012 Q2 to 2014 Q4 and post-KAS from 2015 Q1 to 2020 Q4). We defined slope difference as the difference in the slopes of procurement or discard rate from pre- and post-KDPI implementation periods or pre- and post-KAS introduction periods. Level change is the step difference in the procurement or discard rate at the date of KDPI introduction or KAS implementation. Figure S1 graphically explains the ITS metrics. All inference testing was 2-sided with a significance level of $p < .05$ with the use of the Hochberg multiple comparison testing method.[20] When examining transplantation rates of AKI kidneys by transplant centers, we excluded pediatric transplant centers. Analyses were conducted in SAS, version 9.4 (SAS Institute, Inc).

3 | RESULTS

3.1 | Trends in the characteristics of the deceased-donor pool

The number of all study-eligible deceased kidney donors with at least one kidney procured for transplant purposes increased from 6841 in 2010 to 11 493 in 2020. Changes in the demographic characteristics of study-eligible deceased donors before and after KAS implementation can be seen in Figure 2A,B. The proportion of

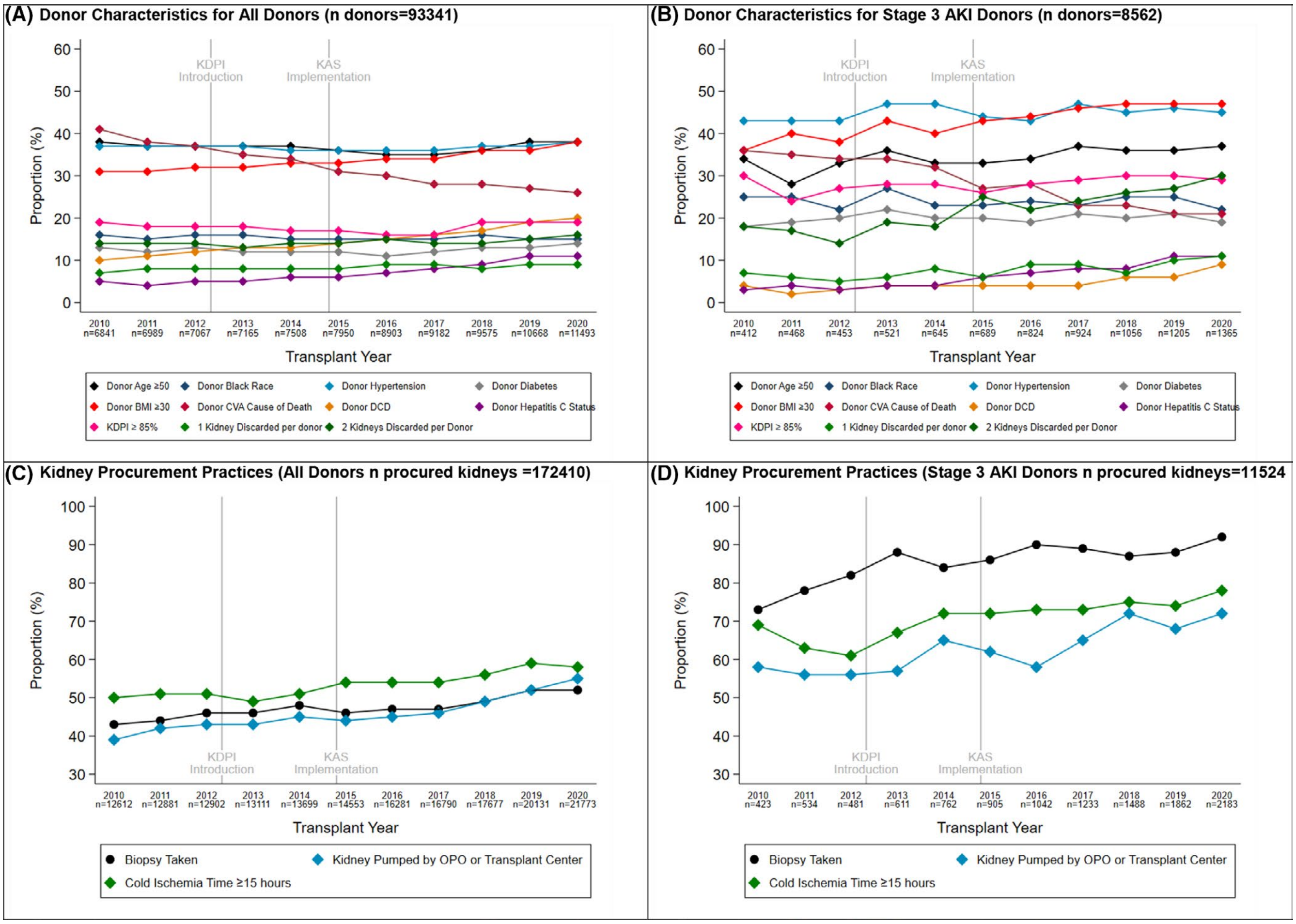

FIGURE 2 Donor characteristics (A, B) and kidney procurement practices (C, D) among the deceased donor pool from 2010 to 2020. Donor characteristics are presented for all donors (A) and Stage 3 AKI donors (B). Kidney procurement practices are presented for all donors (C) and Stage 3 AKI donors (D). Points represent proportions. BMI, body mass index; CVA, cerebrovascular; DCD, donor after cardiac death; KAS, Kidney Allocation System; KDPI, Kidney Donor Profile Index; OPO, organ procurement organization. Cold ischemia time was dichotomized at the median time of 15 h

donors with the following characteristics increased from 2010 to 2020: hepatitis C serostatus (5%–11%), obesity (31%–38%), terminal SCr ≥3 mg/dl (7%–14%), and cardiac determination of death (10%–20%), *p*-values <.05 for all (Figure 2A). The proportion of donors with donation after cardiac determination of death (DCD) increased among all stages of AKI from 2010 to 2020 (Table S2, Table S4A). Donor race/ethnicity, diabetes status, and hypertension status did not change significantly during this timeframe. Of the 93 341 deceased donors, 33 682 (36%) experienced AKI. The proportion of deceased donors with any AKI remained consistent during the study period (38% in 2010 to 37% in 2020), while the proportion of donors with stage 3 AKI increased from 6% in 2010 to 12% in 2020. Stage 3 AKI accounted for a growing proportion of donors with high terminal SCr (>3 mg/dl), increasing from 66% (326/491) in 2010 to 74% (1228/1657) in 2020 (Table 1). The characteristics of donors with stage 3 AKI have shown increases in age, BMI, DCD status, and HCV seropositivity. Average terminal SCr values among donors with stage 3 AKI increased from 4.7 (2.45) mg/dl in 2010 to 5.49 (2.54) mg/dl in 2020 mg/dl (Figure 2B; Table S4C).

From 2010 to 2020, procured kidneys were statistically significantly more likely to be machine-perfused (39%–55%), biopsied (43%–52%), and have prolonged cold ischemia times (≥15 h; 50%–58%) (Figure 2C; Table S4B). Biopsy rates, perfusion rates, and cold ischemia times also increased among procured stage 3 AKI kidneys from 2010 to 2020. Biopsy rates increased from 73% in 2010 to 92% in 2020 (Figure 2D; Table S4D).

3.2 | Trends in the procurement of kidneys for transplantation from AKI donors

A total of 172 410 kidneys were procured for transplantation during the study timeframe. The number of deceased-donor kidneys procured increased from 12 612 in 2010 to 21 773 in 2020 (procurement proportion increased from 92.2% in 2010 to 94.7% in 2020). AKI kidneys accounted for 34% (57 839/172 410) of the kidneys procured during the timeframe. The proportions of kidneys procured remained stable from 2010 to 2020 among deceased donors without

TABLE 1 Number and percentage of donors with stages of AKI by levels of terminal serum creatinine from 2010 to 2020

	Year										
	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Among terminal SCr >3 mg/dl	N = 491	N = 542	N = 567	N = 614	N = 740	N = 843	N = 996	N = 1133	N = 1307	N=1478	N = 1657
No AKI	36 (7%)	41 (8%)	45 (8%)	51 (8%)	56 (8%)	66 (8%)	63 (6%)	76 (7%)	90 (7%)	91 (6%)	99 (6%)
Stage 1 AKI	62 (13%)	55 (10%)	61 (11%)	60 (10%)	59 (8%)	75 (9%)	91 (9%)	86 (8%)	112 (9%)	126 (9%)	144 (9%)
Stage 2 AKI	67 (14%)	82 (15%)	87 (15%)	72 (12%)	99 (13%)	110 (13%)	128 (13%)	154 (14%)	169 (13%)	185 (13%)	186 (11%)
Stage 3 AKI	326 (66%)	364 (67%)	374 (66%)	431 (70%)	526 (71%)	592 (70%)	714 (72%)	817 (72%)	936 (72%)	1076 (73%)	1228 (74%)
Among terminal SCr >2 mg/dl	N = 1032	N = 1094	N = 1097	N = 1148	N = 1326	N = 1435	N = 1740	N = 1879	N = 2102	N = 2392	N = 2723
No AKI	80 (8%)	102 (9%)	98 (9%)	111 (10%)	101 (8%)	126 (9%)	117 (7%)	146 (8%)	161 (8%)	176 (7%)	211 (8%)
Stage 1 AKI	332 (32%)	308 (28%)	320 (29%)	316 (28%)	337 (25%)	357 (25%)	458 (26%)	451 (24%)	513 (24%)	581 (24%)	691 (25%)
Stage 2 AKI	239 (23%)	262 (24%)	258 (24%)	236 (21%)	290 (22%)	298 (21%)	371 (21%)	393 (21%)	413 (20%)	473 (20%)	488 (18%)
Stage 3 AKI	381 (37%)	422 (39%)	421 (38%)	485 (42%)	598 (45%)	654 (46%)	794 (46%)	889 (47%)	1015 (48%)	1162 (49%)	1333 (49%)

Abbreviations: AKI, acute kidney injury; SCr, serum creatinine.

AKI, with stage 1 AKI, and with stage 2 AKI (Table 2, Figure 3A,B). The procurement proportion increased among donors with stage 3 AKI from 51.3% (423/824) in 2010 to 80.0% (2183/2730) in 2020. The number of OPOs that did not procure any kidneys with stage 3 AKI decreased from 3 in 2010 to 1 in 2020.

Figure 4A,B show ITS analysis of procurement rates following KDPI introduction and KAS implementation by stages of AKI, respectively. The adjusted level change (95% confidence interval [CI]) with KDPI introduction on the procurement rate—illustrated in Figure 4A by an upward or downward step change after the first quarter (March) of 2012—were as follows: −1.2 (−2.2, −0.2) for kidneys without AKI, −1.7 (−4.0, 0.5) for stage 1 AKI kidneys, 3.4 (−2.7, 9.5) for stage 2 AKI kidneys, and −3.3 (−11.6, 5.0) among stage 3 AKI kidneys following KDPI introduction (Table S3A). These correspond to slope differences (95% CI) of 0.09 (−0.14, 0.32) among kidneys without AKI, 0.21 (−0.24, 0.66) for stage 1 AKI kidneys, −0.35 (−1.19,0.48) for stage 2 AKI kidneys, and −0.39 (−1.89, 1.11) for stage 3 AKI kidneys (Figure S1). The adjusted level changes (95% CI) in procurement rate following KAS implementation were −1.1 (−4.4, 2.2) for kidneys without AKI, −2.6 (−7.2, 2.0) for stage 1 AKI, 0.3 (−6.8, 7.4) for stage 2 AKI, and −0.3 (−9.2, 8.6) among stage 3 AKI kidneys (Figure 4B; Table S3B). These correspond to slope differences (95% CI) of 0.05 (−0.28, 0.38) among kidneys without AKI, 0.07 (−0.54, 0.68) among stage 1 AKI, 0.82 (−0.4, 2.03) among stage 2 AKI kidneys, and 0.1 (−2.33, 2.54) among stage 3 AKI kidneys.

3.3 | Trends in the discard of kidneys procured for transplant from AKI donors

Among the 172 410 kidneys procured, 137 426 (80%) were transplanted and the remaining 34 984 (20%) were discarded. The number of discarded deceased-donor kidneys increased from 2451 in 2010 to 4785 in 2020 but the overall discard rate increased from 19.4% (2451/12612) in 2010 and 22.0% (4785/21773) in 2020 (Table 2). Kidneys from deceased donors with AKI accounted for 50% (17 559/34 984) of kidneys discarded over the study period. The discard rate did not statistically significantly change for kidneys from donors without AKI or donors with stage 1 AKI from 2010 to 2020 (Table 2, Figure 3C,D). Discard of kidneys from donors with stage 2 AKI increased from 29.2% (268/919) in 2010 to 33.9% (503/1485) in 2020. Discard of kidneys from donors with stage 3 AKI increased from 41.4% (175/423) in 2010 to 44.0% (960/2183) in 2020.

Interrupted time series analysis of kidney discard following KDPI introduction and KAS implementation by stages of AKI can be seen in Figure 4C,D as an upward or downward step change in March 2012 and January 2015, respectively. The slope differences for stage 3 AKI kidneys following KDPI and KAS implementation and are shown in Table S3A,B, respectively. There were no statistically significant changes in discard by KDPI or KAS implementation.

TABLE 2 Number of kidneys procured and discarded by stages of AKI from 2010 to 2020

	Year										
	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Total available donors	6841	6989	7067	7165	7508	7950	8903	9182	9575	10 668	11 493
N (%) kidneys											
Procured[a]	12 612 (92%)	12 881 (92%)	12 902 (91%)	13 111 (91%)	13 699 (91%)	14 553 (92%)	16 281 (91%)	16 790 (91%)	17 677 (92%)	20 131 (94%)	21 773 (95%)
Discarded[b]	2451 (19%)	2460 (19%)	2549 (20%)	2527 (19%)	2721 (20%)	2948 (20%)	3429 (21%)	3354 (20%)	3543 (20%)	4217 (21%)	4785 (22%)
No AKI											
N (%) of donors[c]	4243 (62%)	4381 (63%)	4587 (65%)	4608 (64%)	4788 (64%)	5192 (65%)	5793 (65%)	5984 (65%)	6012 (63%)	6799 (64%)	7272 (63%)
N available kidneys	8486	8762	9174	9216	9576	10 384	11 586	11 968	12 024	13 598	14 544
N (%) kidneys											
Procured[a]	8186 (96%)	8402 (96%)	8739 (95%)	8806 (96%)	9158 (96%)	9915 (95%)	11 082 (96%)	11 403 (95%)	11 553 (96%)	13 198 (97%)	14 129 (97%)
Discarded[b]	1222 (15%)	1306 (16%)	1397 (16%)	1330 (15%)	1373 (15%)	1496 (15%)	1748 (16%)	1671 (15%)	1658 (14%)	2026 (15%)	2198 (16%)
Stage 1 AKI											
N (%) of donors[c]	1674 (24%)	1599 (23%)	1511 (21%)	1551 (22%)	1539 (20%)	1514 (19%)	1637 (18%)	1638 (18%)	1801 (19%)	1900 (18%)	2083 (18%)
N available kidneys	3348	3198	3022	3102	3078	3028	3274	3276	3602	3800	4166
N (%) kidneys											
Procured[a]	3084 (92%)	2967 (93%)	2730 (90%)	2826 (91%)	2826 (92%)	2747 (91%)	2975 (91%)	3023 (92%)	3340 (93%)	3618 (95%)	3976 (95%)
Discarded[b]	786 (25%)	698 (24%)	723 (26%)	710 (25%)	714 (25%)	757 (28%)	858 (29%)	791 (26%)	879 (26%)	942 (26%)	1124 (28%)
Stage 2 AKI											
N (%) of donors[c]	512 (7.5%)	541 (7.7%)	516 (7.3%)	485 (6.8%)	536 (7.1%)	555 (7%)	649 (7.3%)	636 (6.9%)	706 (7.4%)	764 (7.2%)	773 (6.7%)
N available kidneys	1024	1082	1032	970	1072	1110	1298	1272	1412	1528	1546
N (%) kidneys											
Procured[a]	919 (90%)	978 (90%)	952 (92%)	868 (89%)	953 (89%)	986 (89%)	1182 (91%)	1131 (89%)	1296 (92%)	1453 (95%)	1485 (96%)
Discarded[b]	268 (29%)	271 (28%)	276 (29%)	253 (29%)	349 (37%)	311 (32%)	390 (33%)	375 (33%)	387 (30%)	490 (34%)	503 (34%)
Stage 3 AKI											
N (%) of donors[c]	412 (6%)	468 (6.7%)	453 (6.4%)	521 (7.3%)	645 (8.6%)	689 (8.7%)	824 (9.3%)	924 (10.1%)	1056 (11%)	1205 (11.3%)	1365 (11.9%)
N available kidneys	824	936	906	1042	1290	1378	1648	1848	2112	2410	2730
N (%) kidneys											
Procured[a]	423 (51%)	534 (57%)	481 (53%)	611 (59%)	762 (59%)	905 (66%)	1042 (63%)	1233 (67%)	1488 (70%)	1862 (77%)	2183 (80%)
Discarded[b]	175 (41%)	185 (35%)	153 (32%)	234 (38%)	285 (37%)	384 (42%)	433 (42%)	517 (42%)	619 (42%)	759 (41%)	960 (44%)

Abbreviation: AKI, acute kidney injury.

[a]Procurement rate was calculated as the number of kidneys procured over the number of available kidneys from eligible donors.

[b]Discard was calculated as the number of kidneys that were ultimately not utilized over the number of kidneys procured for transplantation.

[c]The proportion of donors with no AKI, stage 1, stage 2, or stage 3 AKI was calculated as the number of donors with the corresponding AKI status over the total number of eligible donors from the deceased donor pool that year.

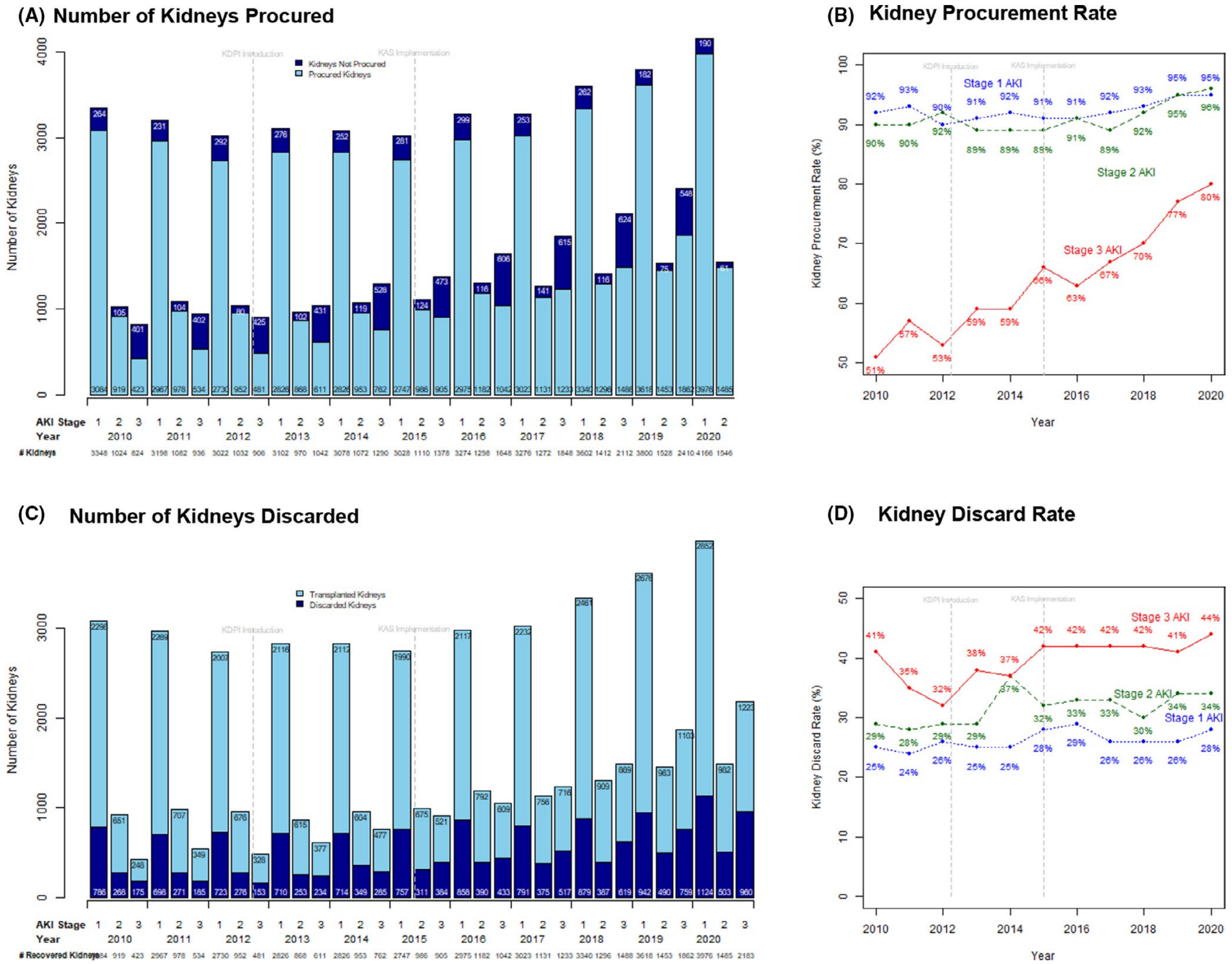

FIGURE 3 Trends in kidney procurement (A, B) and discard (C, D) by stages of AKI from 2010 to 2020: (A, C) absolute counts of the number of kidneys procured and discarded from 2010 to 2020 by stages of AKI and (B, D) proportion of kidneys procured and discarded from 2010–2020 by stages of AKI. AKI, acute kidney injury

3.4 | Transplant center-level trends

The number of transplant centers that used stage 3 AKI kidneys increased from 87/243 (36%) in 2010 to 137/243 (56%) in 2020. The proportion of transplant centers with high stage 3 AKI kidney utilization (>5% of all their transplants that year) increased from 13% (35/243) in 2010 to 32% (78/243) in 2020 (Table 3).

4 | DISCUSSION

From 2010 to 2020, the proportion of referred donors with stage 3 AKI and the procurement rate of stage 3 AKI kidneys increased significantly. The discard rate of stage 3 AKI kidneys dropped from 41% in 2010 to 32% in 2012 before increasing to 44% in 2020, a rise that coincided with the introduction of KDPI and implementation of KAS. Increases in the utilization of stage 3 AKI kidneys at the transplant center level appear to be driven by a small proportion of transplant centers (centers with >5% of their transplants each year from stage 3 AKI kidneys) that have aggressively utilized these kidneys, as the majority of centers use relatively few stage 3 AKI kidneys.

The observed increases in the proportion of deceased donors with stage 3 AKI may be partially explained by increasing prevalence of risk factors including obesity, circulatory determination of death, sepsis, acute heart failure, and increased rates of cardiac catheterization and mechanical ventilation.[21] The incidence of severe AKI among hospitalized patients has been rising and thus the increasing prevalence of AKI among deceased donors is not unexpected.[21] On the other hand, it is also possible that some temporal trends observed here are due to changes in the aggressiveness of OPOs over time, such that some OPOs pursued donors with higher KDPIs and reported these donors to UNOS.

Despite the possibly higher comorbidity profile, cohort and registry-based findings support the use of AKI kidneys. However,

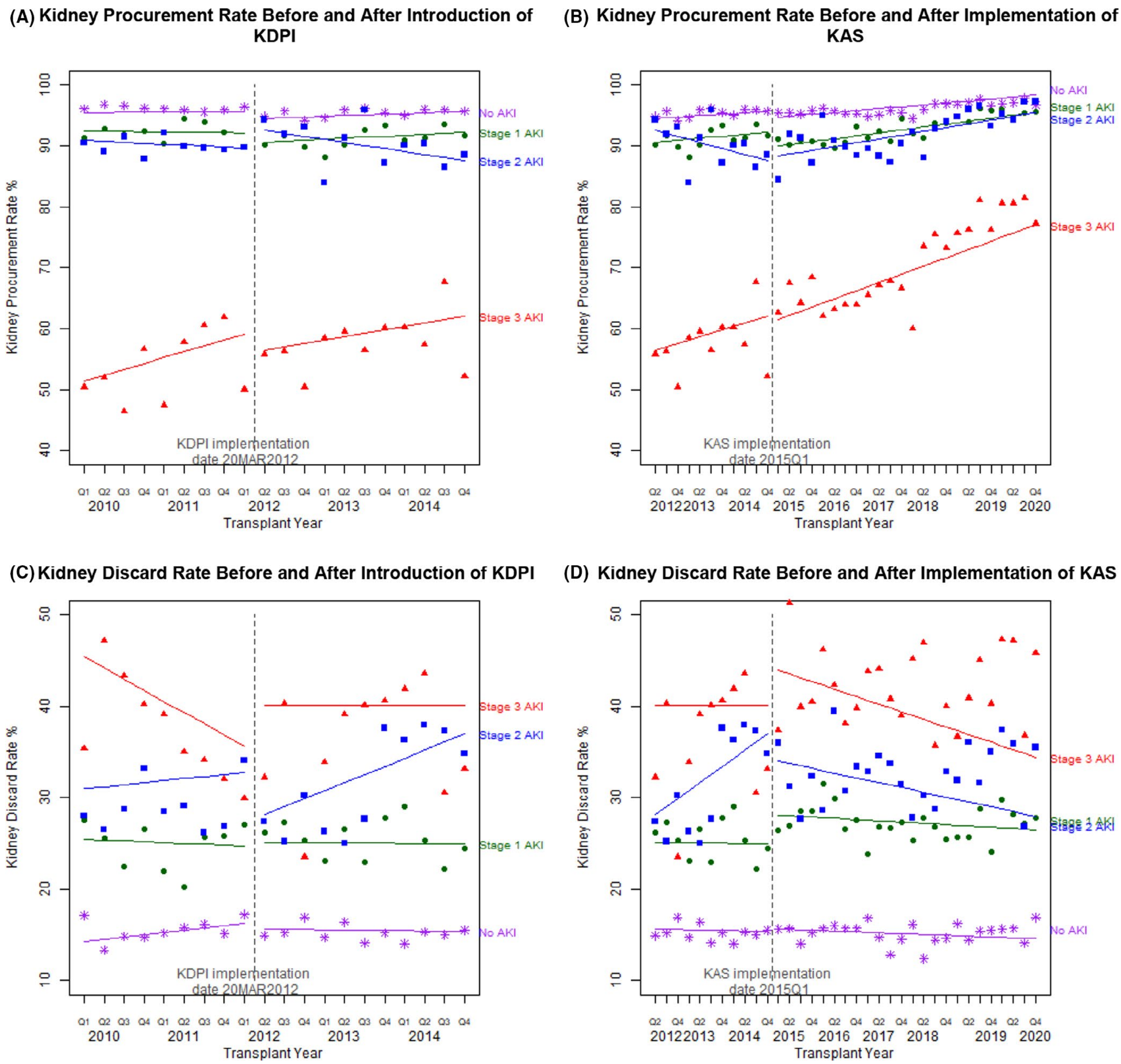

FIGURE 4 Interrupted time series (ITS) of kidney procurement (A, B) and discard (C, D) by stages of AKI after Introduction of KDPI (A, C) and implementation of KAS (B, D). Points represent observed rates per quarter. Lines represent predicted rates from ITS analysis. The dotted vertical lines indicate the introduction of KDPI (A, C) or the implementation of KAS (B, D). AKI, acute kidney injury; KAS, Kidney Allocation System; KDPI, Kidney Donor Profile Index. See Table S3 for ITS effect estimates and Figure S1 for a graphical explanation of ITS

our study identified that nearly half of all discarded kidneys from 2010 to 2020 were from donors with AKI. In a review of 28 cohort and registry-based studies on AKI and graft failure, 25 studies found no association between AKI and graft failure.[12] Findings from the remaining three studies may be attributed to different practices in the United Kingdom compared to the United States[22,23] as well as restricted settings in intensive care[24] and ECDs.[25] A propensity score-matched US registry study detected no association between AKI and graft failure, even in the most severe instances of AKI.[11] The comparable rates of graft survival between AKI and non-AKI kidneys have been hypothesized to be the result of fluid losses and hemodynamic changes from vasopressin fluctuations during brain death, resulting in high terminal SCr that may not be indicative of intrinsic tissue injury.[26–28] AKI kidneys, including stage 3 AKI kidneys, may be a viable and underutilized group of deceased-donor kidneys.

The discard rate of stage 3 AKI kidneys decreased from 2010 to 2012 before increasing until the end of 2020, coinciding with the introduction of KDPI in 2012 and subsequent KAS implementation in 2014. Increased procurement and discard rates have led to proportionately less utilization, although the absolute number of

TABLE 3 Number of transplant centers[a] by proportion of at least stage 2 or stage 3 AKI kidney transplants

	Transplant year										
	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Number (%) of transplant centers by proportion of ≥ stage 2 AKI kidney transplants											
0% ≥ stage 2 AKI	52 (21%)	57 (23%)	56 (23%)	56 (23%)	58 (24%)	58 (24%)	49 (20%)	51 (21%)	41 (17%)	45 (19%)	45 (19%)
0%-5% ≥ stage 2 AKI	60 (25%)	64 (26%)	61 (25%)	73 (30%)	65 (27%)	56 (23%)	65 (27%)	57 (23%)	55 (23%)	57 (23%)	52 (21%)
>5% ≥ stage 2 AKI	131 (54%)	122 (50%)	126 (52%)	114 (47%)	120 (49%)	129 (53%)	129 (53%)	135 (56%)	147 (60%)	141 (58%)	146 (60%)
Number (%) of transplant centers by proportion of stage 3 AKI kidney transplants											
0% stage 3 AKI	156 (64%)	152 (63%)	159 (65%)	150 (62%)	137 (56%)	131 (54%)	136 (56%)	126 (52%)	111 (46%)	120 (49%)	106 (44%)
0%-5% stage 3 AKI	56 (23%)	50 (21%)	54 (22%)	50 (21%)	63 (26%)	64 (26%)	61 (25%)	61 (25%)	58 (24%)	48 (20%)	59 (24%)
>5% stage 3 AKI	31 (13%)	41 (17%)	30 (12%)	43 (18%)	43 (18%)	48 (20%)	46 (19%)	56 (23%)	74 (30%)	75 (31%)	78 (32%)

Abbreviation: AKI, acute kidney injury.

[a]A total of 17 pediatric transplant centers were excluded; 243 transplant centers were included.

kidneys utilized has increased. A subsequent ITS analysis, a quasi-experimental design that evaluates the effect of an intervention, confirmed that the decline in the discard rate of stage 3 AKI kidneys prior to 2012 and increase after KAS implementation or KDPI introduction was not statistically significant. Our findings, although not statistically significant, suggest there may be a KDPI "labeling effect" where viable kidneys with high KDPI scores are less likely to be accepted by patients and transplant centers.[5] This labeling effect may be most evident for KDPI >85% kidneys, since receiving offers for such kidneys requires explicit, written consent from the patient.[2] In fact, most (~70%) high terminal SCr values are from donors with stage 3 AKI—and disproportionately more likely to discarded.[29] For example, in a 41-year-old, Black donor with hypertension and diabetes, without HCV and DCD, with a cerebrovascular cause of death, and stage 3 AKI, calculations based on his terminal SCr of 6.6 mg/dl generates a KDPI of 85 compared to his lowest SCr value in DonorNet of 0.9 mg/dl which generates a KDPI of 70. The resulting high KDPI scores driven by high terminal SCr due to AKI status may have increased the discard of viable AKI kidneys—without significant improvement in the performance of the KDPI.[9] Additional possible contributors to lower utilization include fear of poor outcomes, potential increased resource utilization coupled with non-reimbursement, and other constrains in such allocation practices.

Alternatively, the advent of KDPI and KAS may have supported a more aggressive pursuit of donor kidneys. As such, KDPI and/or KAS implementation may have mediated the observed increases in stage 3 AKI discard rate. These two seemingly paradoxical trends—the rise in stage 3 AKI kidney discard rate, concurrent with an increase in the number of centers transplanting these kidneys—are likely due to increased procurement of stage 3 AKI kidneys that outpaces utilization. In addition, prior studies have identified the existence of aggressive centers that consistently use suboptimal grafts.[30] Aggressive centers, defined in our study as transplant centers with >5% of their transplants from stage 3 AKI kidneys, comprise a small, growing proportion of US transplant centers. The majority of transplant centers use few stage 3 AKI kidneys, and almost half of all US transplant centers did not use any stage 3 AKI kidneys in 2020. The influx of procured stage 3 AKI kidneys has also coincided with increased usage of kidney hypothermic machine perfusion and longer cold ischemia times, the former of which has been identified as a significant buffer in preventing discard.[31] As the transplant system faces a steady influx of kidneys, mock organ offer simulation studies including UNOS's DonorNet simulator, SimUNet, could help forecast behavioral changes in organ offer acceptance practice as OPOs procure more complex kidneys, including those from donors with AKI.[32] Further utilization of stage 3 AKI kidneys may be assisted by availability of repair biomarkers like YKL-40 or uromodulin and osteopontin that are associated with improved long-term graft outcomes in recipients.[33,34]

There are several strengths and limitations to consider in our study. First, we used national registry data from 2010 to 2020 to characterize trends in deceased-donor kidney procurement and allocation practices in the US. Use of DonorNet provided serial SCr measurements to more closely align AKI definitions with established definitions and includes all solid organ donors—regardless of whether they a kidney was procured or not. To our knowledge, this is the first study to characterize national trends in the procurement and utilization of AKI kidneys from deceased donors using this definition of AKI. Finally, the use of ITS analyses accounted for underlying trends in donor demographics and kidney allocation practices, as well as secular trends.[19] Limitations to our study include lack of urine output to define AKI according to KDIGO guidelines. In addition, use of the lowest SCr on admission as the baseline to calculate AKI may have underestimated the true number of stage 3 AKI kidneys as events prior to hospitalization may elevate SCr. Furthermore, the ITS analyses assume a lack of competing interventions during the study timeframe. Sample sizes are also much smaller for stage 3 AKI group, which limits the power to detect potentially real effects. This limitation may explain why some apparently large effects upon visual examination are statistically insignificant (i.e., stage 3 AKI). Finally, the final year of the study (2020) was impacted immensely by COVID-19, particularly as kidney discard rates spiked at the start of the pandemic. Data points from early 2020 may serve as leverage/influence points in ITS analyses.

In conclusion, we found statistically insignificant increases in the procurement and discard rates of stage 3 AKI kidneys following implementation of KAS. Although the discard rate has increased, the absolute number of stage 3 AKI kidneys transplants has increased and the number of transplant centers utilizing stage 3 AKI kidneys has increased from 33% to over half. This may reflect increased center adoption and experience with stage 3 AKI kidneys with continued room for improvement in organ utilization.

ACKNOWLEDGMENTS

The data reported here have been supplied by the United Network for Organ Sharing (UNOS) as the contractor for the OPTN. The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by the OPTN or the US Government. The content is the responsibility of the authors alone and does not necessarily reflect the view or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the US Government. These organizations were not involved in study design, analysis, interpretation, or manuscript creation.

DISCLOSURE

The authors of this manuscript have conflicts of interest to disclose as described by the *American Journal of Transplantation*. S. Alasfar reports grant support from CareDx, Shire, and NIH. P.P. Reese reports epidemiology consulting for VALHeath related to identifying patients with chronic kidney disease; Investigator-initiated and collaborative grants from Merck, Gilead, and AbbVie to the University of Pennsylvania to support trials of transplanting organs from donors with Hepatitis C into Hepatitis C negative recipients; and serves as an Associate Editor of the American Journal of Kidney Disease. S. Mohan reports grant/research support from NIH (NIDDK/NIAID/NIHMD/NIBIB), consulting fees from Angion Pharmaceuticals and serves as Deputy Editor of Kidney International Reports. M.D. Doshi reports salary support from NIDDK. I.E. Hall reports NIH grant support from NCATS (UL1TR002538 and KL2TR002539). C.R. Parikh reports consulting fees from Renalytix (Advisory Board) and Genfit (DSMB), grant/research support from National Institute of Diabetes and Digestion and Kidney Diseases, National Heart, Lung, and Blood Institute. All other co-authors have no disclosures as described by the *American Journal of Transplantation*.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available via request to the Organ Procurement and Transplantation Network (OPTN).

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Liu C, Alasfar S, Reese PP, et al. Trends in the procurement and discard of kidneys from deceased donors with acute kidney injury. *Am J Transplant*. 2022;22:898–908. doi:10.1111/ajt.16920