# Influence of Cold Ischemia Time in Combination with Donor Acute Kidney Injury on Kidney Transplantation Outcomes

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**BACKGROUND:** Deceased-donor kidneys are often exposed to ischemic events from donor instability, as evidenced by acute kidney injury (AKI). Clinicians may be reluctant to transplant kidneys with AKI that also have prolonged cold ischemia time (CIT) for fear of an additional deleterious effect.

**STUDY DESIGN:** We evaluated national data between 1998 and 2013 of adult first-time kidney-only recipients of paired kidneys from donors with AKI (terminal serum creatinine $\geq$ 2 mg/dL), in which the CIT difference between recipients was $\geq$1, 5, 10, or 15 hours.

**RESULTS:** On multivariate analysis of AKI kidney recipients, overall death-censored graft survival (DCGS) was comparable between recipients with higher CIT relative to paired donor recipients with lower CIT when the CIT difference was at least 1 hour (adjusted hazard ratio [aHR] 0.98, 95% CI 0.85 to 1.13, n = 4,458), 5 hours (aHR 0.97, 95% CI 0.79 to 1.18, n = 2,412), 10 hours (aHR 0.82, 95% CI 0.59 to 1.15, n = 922), or 15 hours (aHR 0.94, 95% CI 0.57 to 1.58, n = 442). Overall patient survival of the longer CIT groups was comparable or protective with delta CIT of $\geq$1 (aHR 0.94, 95% CI 0.83 to 1.06), 5 (aHR 0.80, 95% CI 0.68 to 0.94), 10 (aHR 0.70, 95% CI 0.53 to 0.91), and 15 (aHR 0.64, 95% CI 0.43 to 0.95) hours. Between each of the 4 delta-CIT levels of shorter and longer CIT, there were no statistically significant differences in the proportion of acute rejection at delta $\geq$1, 5, 10, or 15 hours.

**CONCLUSIONS:** These results suggest that in the setting of a previous ischemic donor event, prolonged CIT has limited bearing on long-term outcomes. This may be important evidence that despite the occurrence of other ischemic events, kidneys with prolonged CIT offer acceptable outcomes to recipients and are a potential source to expand the donor pool. (J Am Coll Surg 2015;221:532–538. © 2015 by the American College of Surgeons)

As the disparity between kidney need and availability continues to widen, efforts to reduce kidney discard are critically important. Placement of deceased-donor kidneys to centers outside of the local donor service area offers the potential to reduce discard; however, kidney placement is often delayed because of time required to find an accepting center.[1] This leads to prolonged cold ischemia time (CIT), which may contribute to the ultimate discard of the kidney. Additionally, deceased-donor kidneys are often subjected to other ischemic events such as hypoxia/hypoperfusion, as evidenced by acute kidney injury (AKI). Based on the response-to-injury hypothesis,[2,3] early injury from ischemia may set the stage for indolent yet chronically progressive damage leading to higher rates of chronic graft loss. Therefore, clinicians may be reluctant to accept kidneys with a long CIT that also have been subjected to other ischemic events for fear of an additional deleterious effect. In fact, previous reports indicate restriction of CIT to 18 to 30 hours[4,5] when transplanting AKI kidneys.

**Disclosure Information: Nothing to disclose.**

Disclaimer: The data reported here were supplied by the Minneapolis Medical Research Foundation as the contractor for the Scientific Registry of Transplant Recipients (SRTR). The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy of or interpretation by the SRTR or the US Government.

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**Abbreviations and Acronyms**

aHR = adjusted hazard-ratio
AKI = acute kidney injury
CIT = cold ischemia time
DGF = delayed graft function
HLA = human leukocyte antigen
PCKD = polycystic kidney disease
PRA = panel reactive antibodies
SRTR = Scientific Registry of Transplant Recipients

To analyze the risks associated with transplantation of kidneys with long CIT in combination with AKI, we examined national registry data for outcomes of adult transplant recipients of AKI kidneys in which both kidneys from the same donor were transplanted into separate recipients with different CITs. An analysis of mate kidneys from the same donor is optimal to control for the predominant effects of donor quality while illustrating the effects of CIT.

## METHODS

### Sources of data

We used data from the Scientific Registry of Transplant Recipients (SRTR). The SRTR data system includes data on all donors, wait-listed candidates, and transplant recipients in the US, submitted by the members of the Organ Procurement and Transplantation Network (OPTN). The Health Resources and Services Administration, U.S. Department of Health and Human Services provides oversight to the activities of the Organ Procurement and Transplantation Network and SRTR contractors. This study was approved by the Institutional Review Board of the Albert Einstein College of Medicine.

### Study population

We examined data from the SRTR on all adult, first-time, deceased-donor, kidney-only recipients, between January 1998 and October 2013, with a common donor who had acute kidney injury (AKI, defined as terminal serum creatinine $\geq$ 2 mg/dL). Recipient outcomes were compared between paired donors stratified by CIT group; the kidney with the shorter CIT was placed in the short-CIT group and its mate with the longer CIT in the long-CIT group, according to CIT differences (delta-CIT) of at least 1 hour, $\geq$5 hours, $\geq$10 hours, and $\geq$15 hours. Exclusions were previous organ transplant, hepatitis C or human immunodeficiency virus positivity, research study participation, and missing information on CIT or terminal serum creatinine. Paired donors were categorized using a donor identifier available in the registry.

### Outcomes

The primary outcome was time to death-censored graft survival (DCGS, defined as return to chronic dialysis,

**Table 1.** Recipient Characteristics by Change in Cold Ischemia Time

| | Delta CIT $\geq$ 1 h (n = 4,458) | | Delta CIT $\geq$ 5 h (n = 2,412) | | Delta CIT $\geq$ 10 h (n = 922) | | Delta CIT $\geq$ 15 h (n = 442) | |
|---|---|---|---|---|---|---|---|---|
| **Characteristic** | **Shorter CIT** | **Longer CIT** | **Shorter CIT** | **Longer CIT** | **Shorter CIT** | **Longer CIT** | **Shorter CIT** | **Longer CIT** |
| Age, y, mean ± SD | 53.1 ± 13.0 | 53.4 ± 12.7 | 52.8 ± 13.1 | 53.3 ± 12.8 | 53.0 ± 13.3 | 53.6 ± 12.7 | 53.1 ± 13.4 | 53.5 ± 12.9 |
| Black ethnicity, % | 33.9 | 33.7 | 35.5 | 34.3 | 35.6 | 34.7 | 35.8 | 34.8 |
| Male, % | 61.8 | 62.6 | 59.9 | 62.9 | 61.4 | 64.0 | 57.5 | 62.9 |
| Diabetes mellitus, % | 30.9 | 32.7 | 30.5 | 32.3 | 30.2 | 35.1 | 31.7 | 36.2 |
| PCKD, % | 10.0 | 9.2 | 10.3 | 7.8 | 9.3 | 8.0 | 9.5 | 6.3 |
| Pre-transplantation dialysis > 36 mo, % | 54.1 | 53.8 | 52.4 | 54.7 | 51.7 | 58.5 | 47.0 | 59.4 |
| Comorbidity, % | 17.3 | 16.6 | 15.3 | 15.5 | 16.3 | 13.9 | 17.7 | 15.8 |
| BMI > 30 kg/m$^2$, % | 34.8 | 34.8 | 34.3 | 35.9 | 35.0 | 37.4 | 35.6 | 41.8 |
| PRA > 30%, % | 16.5 | 16.6 | 17.0 | 17.6 | 17.9 | 16.9 | 17.4 | 14.6 |
| Nonprivate insurance, % | 73.5 | 71.2 | 73.1 | 71.9 | 72.9 | 72.9 | 74.2 | 75.6 |
| Donor: recipient weight ratio, mean ± SD | 1.13 ± 0.40 | 1.12 ± 0.38 | 1.15 ± 0.40 | 1.13 ± 0.38 | 1.13 ± 0.38 | 1.12 ± 0.37 | 1.11 ± 0.36 | 1.10 ± 0.36 |
| HLA mismatches >3, % | 73.4 | 74.8 | 72.3 | 74.9 | 78.9 | 72.2 | 71.0 | 69.2 |
| Machine perfusion, % | 40.0 | 41.0 | 39.2 | 40.6 | 42.5 | 45.3 | 40.7 | 42.1 |
| Nonlocal donor, % | 28.3 | 35.5 | 27.5 | 39.3 | 27.3 | 47.5 | 28.5 | 57.5 |
| Median CIT, % | 16.6 | 23.5 | 16.0 | 26.0 | 16.1 | 33.0 | 14.0 | 35.0 |

Data not shown for cases with missing BMI (n = 421), PRA (n = 63), and dialysis duration (n = 54).
CIT, cold ischemia time; HLA, human leukocyte antigen; PCKD, polycystic kidney disease; PRA, panel reactive antibody.