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Analyzing the Impact of CIT on the Largest Reported Cohort of Robotic Kidney Transplantation From the Deceased Donors

Egor Petrochenkov, MD,[1] Giulia Bencini, MD,[1] Alessandro Martinino, MD,[1] Amy Lian, MD,[2] Joanna Olazar, BS,[1] Stepan Akshelyan, MD,[1] Kentaro Yoshikawa, MD,[1] Pierpaolo Di Cocco, MD,[1] Jorge Almario-Alvarez, MD,[1] Mario Spaggiari, MD,[1] Enrico Benedetti, MD,[1] and Ivo Tzvetanov, MD[1]

Background. Robotic-assisted kidney transplant (RAKT) has proven to be a successful approach for patients with morbid obesity and more centers are encouraged to apply robotic approach also for deceased donor kidney transplantation. Prolonged cold ischemia time (CIT) is accompanied by delayed graft function (DGF) and early graft loss after traditional open kidney transplant (OKT). This study examines the impact of CIT after robotic kidney transplantation on settings of deceased donation. **Methods.** We present a single-center retrospective analysis of 115 cases of RAKT and 128 cases of OKT from deceased donors performed from deceased donor from 2009 to July 2022. Cohort was divided in 3 groups based on CIT ("high" CIT > 15 h, n = 43; "medium" CIT 11–15 h, n = 38; "low" CIT< 11 h, n = 40). The subgroup analysis of DGF and CIT was performed. **Results.** The median CIT in the cohort was 13.46 (7) h, and overall rate of DGF was 30.6%. The correlation between CIT and DGF was statistically significant ($P = 0.008$), and DGF negatively correlated with 1-y graft survival ($P = 0.04$). The rate of DGF was significantly different between the groups ($P = 0.05$). **Conclusions.** Results from our study demonstrate that the effect of CIT on DGF in settings of RAKT follows a similar pattern as in traditional OKT.

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Recently, the emergence of elective robotic-assisted kidney transplant (RAKT) has proven to be a viable alternative to open kidney transplant (OKT), with benefits such as decreased surgical morbidity.[1] After favorable results with living donor RAKT, more and more centers are encouraged to apply robotic approach to deceased donor kidney transplantation, with results comparable to the traditional surgical technique.[2]

One of the major challenges of deceased organ transplant is its time-sensitive nature.[3] Prolonged cold ischemia time (CIT) is known to be accompanied by delayed graft function (DGF) and early graft loss after traditional open kidney transplant (OKT).[4] The effect of CIT in the setting of robotic kidney transplantation is less certain and has not been studied in detail. This study examines the impact of CIT after robotic kidney transplantation in the setting of deceased donation and compares it with the outcomes after OKT.

MATERIALS AND METHODS

Study Design and Patient Population

A retrospective analysis of RAKT from deceased donors performed from June 2009 to November 2021 was conducted. Per protocol, adult patients (>18 y) were considered eligible for RAKT if they had a body mass index (BMI) ≥35 kg/m^2 at the time of listing but excluded in the presence of significant iliac atherosclerosis. Additionally, patients were assigned to the control group (OKT) if they had pretransplant BMI ≥35 kg/m^2 and received a deceased donor kidney transplant during the same timeframe via traditional open technique due to logistical reasons (a surgeon trained for RAKT was unavailable) or had mentioned above contraindications to the robotic procedure. A modified version of the robotic-assisted transabdominal technique described by our group for transplanting the kidney in the right iliac fossa was adopted.[5] Patients who underwent additional surgical procedures and recipients who underwent simultaneous kidney-pancreas transplantation were excluded from

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[1] Division of Transplantation, Department of Surgery, University of Illinois at Chicago, Chicago, IL.

[2] School of Medicine, University of Illinois at Chicago College of Medicine, Chicago, IL.

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Correspondence: Alessandro Martinino, MD, Department of Surgery, University of Illinois at Chicago, 840 S Wood St, Suite 502, Clinical Science Building Chicago, IL 60612. (alessandro.martinino@uic.edu).

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the analysis. All kidney transplants were performed in the settings of ABO compatibility. Patients from both groups underwent identical immunosuppression protocols, details of which have already been published by our group.[6] Patient demographic information and intraoperative, postoperative, and follow-up data were obtained from the electronic health record. Each recipient had at least 1 y of follow-up. Donor demographic and cause of death, kidney donor profile index (KDPI), type of donation (donation after brainstem death [DBD]/ donation after circulatory death [DCD]), CIT, and for DCD donors, functional warm ischemia time (WIT) and pump data were collected from the OPTN website. DGF was the primary endpoint of the study and was defined as dialysis within the first week of transplantation. Patient and graft survival, as well as graft function, were the secondary endpoint. This study was approved by institutional review board# 2022-1122.

Statistical Analysis

Comprehensive descriptive analyses of all variables were performed. Qualitative variables were presented as counts and percentages and were compared using the chi-square test or Fisher's exact test. Normally distributed quantitative variables were computed as mean ± standard deviation, and non-normally distributed data were presented as median (IQR). A correlation between potential risk factors and DGF was studied using univariate logistic regression, as well as using Pearson Correlation Analysis and Spearman's ρ test. Only variables showing a significance over 0.2 in the correlation and univariate analyses were added into the regression models. Risk factors for DGF were assessed using a probit regression approach. Adjustment was made with covariates, which were significant in correlation analysis or univariate logistic regression ($P < 0.05$), or which were identified as risk factors for DGF in the previous literature. Marginal effects in the regressions were calculated to study the impact of CIT on DGF between the groups. To study CIT in the RAKT group, a cluster analysis was performed. In the clusters, groups of quantitative variables were compared using either an ANOVA or the Kruskal–Wallis test. Secondary pairwise comparisons were assessed using the Dwass, Steel, Critchlow–Fligner multiple comparison procedure. Kidney graft and patient survival rates were computed using the Kaplan–Meier method, comparisons between groups were performed using the log-rank test. All tests were 2-sided, and a P value of <0.05 was the cutoff for significance.

RESULTS

Study Population

Over the study period, 115 cases of RAKT and 128 cases of OKT from deceased donors were performed at the University of Illinois Hospital. Detailed recipient and donor baseline characteristics are presented in Tables 1 and 2, respectively.

The average CIT in was not statistically different between the groups (RAKT versus OKT, 850.6 ± 289.2 versus 868.6 ± 314.4 min; $P = 0.64$). The rate of DGF in the cohort was 30.2% and was comparable between the groups (RAKT versus OKT, 33.2% versus 26.2%; $P = 0.41$).

All DCD donors were placed on a perfusion pump. We performed RAKTs when the robotic surgery team was available, ideally during daytime hours.

Correlation Analysis and Study of CIT in Probit Regressions

CIT positively correlated with DGF in both groups (RAKT and OKT, $r = 0.29$; $P = 0.002$ and $r = 0.22$; $P = 0.013$). A detailed list of parameters that are associated with DGF is presented in Table 3. At the same time, a negative correlation between DGF and 1-y death-censored graft

TABLE 1.

Baseline recipient characteristics stratified by type of surgery

Characteristics	RAKT (n = 115)	OKT (n = 128)	Total (n = 243)	P
Age (y), mean ± SD	47.3 ± 11.3	54.1 ± 10.8	50.1 ± 11.5	0.00[a]
Weight (kg), mean ± SD	131.7 ± 22.3	117.7 ± 18.3	124.3 ± 21.5	0.00[a]
BMI (kg/m^2), mean ± SD	44.2 ± 6.1	40.6 ± 4.3	42.3 ± 5.5	0.00[a]
Male, n (%)	75 (65)	72 (56)	147 (60.2)	0.15
h/o of Heart disease, n (%)	22 (19)	50 (39)	72 (30)	0.00[a]
h/o of Diabetes	50 (43)	80 (62)	130 (53)	0.01

[a]$P > 0.001$.
OKT, open kidney transplant; RAKT, robotic-assisted kidney transplant.

TABLE 2.

Baseline donor characteristics stratified by type of surgery

Characteristics	RAKT (n = 115)	OKT (n = 128)	Total (n = 243)	P
Age (y), mean ± SD	36.7 ± 13.7	40.8 ± 14.9	38.9 ± 14.3	0.03
Weight (kg), mean ± SD	84.3 ± 23.1	85.3 ± 26	84.8 ± 24.6	0.7
Terminal serum creatinine (mg/dL), mean ± SD	1.3 ± 0.8	1.2 ± 1	1.3 ± 0.9	0.7
KDPI, mean ± SD	43.3 ± 24.9	52.2 ± 23.9	48 ± 24.7	0.05
DCD, n (%)	22 (19)	50 (39)	72 (30)	0.00[a]

[a]$P > 0.001$.
DCD, donation after circulatory death; KDPI, kidney donor profile index; OKT, open kidney transplant; RAKT, robotic-assisted kidney transplant.

TABLE 3.

Correlation analysis of potential risk factors of DGF

Characteristics	RAKT (n = 115)		OKT (n = 128)	
	r	*P*	*r*	*P*
Recipient age	0.11	0.23	0.021	0.82
Recipient BMI	0.176	0.06	0.088	0.33
Donor age	0.302	0.00a	0.101	0.26
KDPI	0.272	0.00a	0.028	0.75
WIT	0.144	0.14	0.16	0.08
CIT	0.29	0.00a	0.23	0.013[a]
DCD	0.138	0.141	0.19	0.03[a]
Length of surgery	0.234	0.00*	0.10	0.23

[a]$P > 0.001$.

BMI, body mass index; CIT, cold ischemia time; DCD, donation after circulatory death; KDPI, kidney donor profile index; OKT, open kidney transplant; RAKT, robotic-assisted kidney transplant; WIT, warm ischemia time.

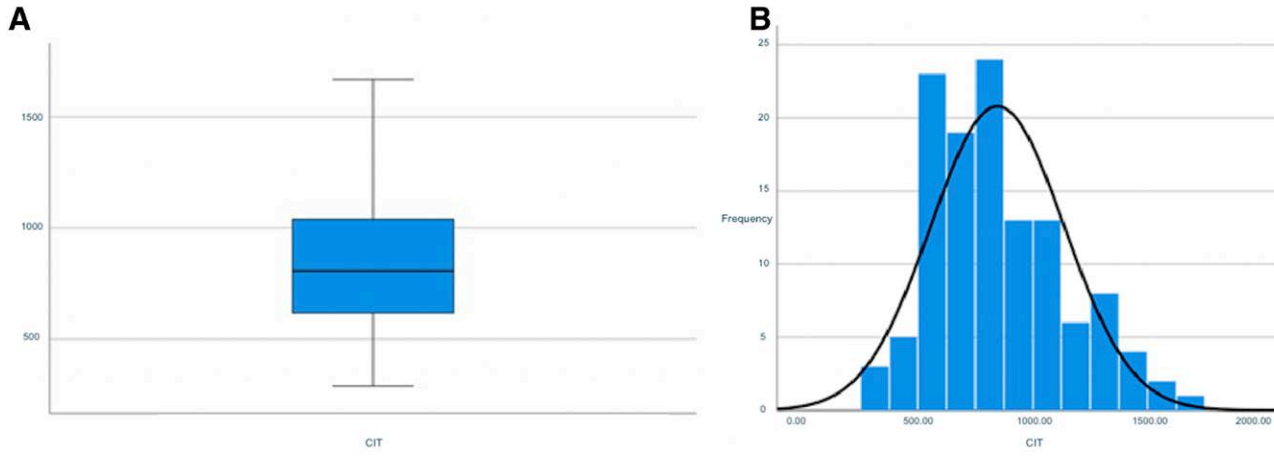

FIGURE 1. Representation of the distribution of cold ischemia time in our cohort. The median CIT is 13.46 h (range: 4.8–27.82 h). A, The box plot. B, The histogram. CIT, cold ischemia time.

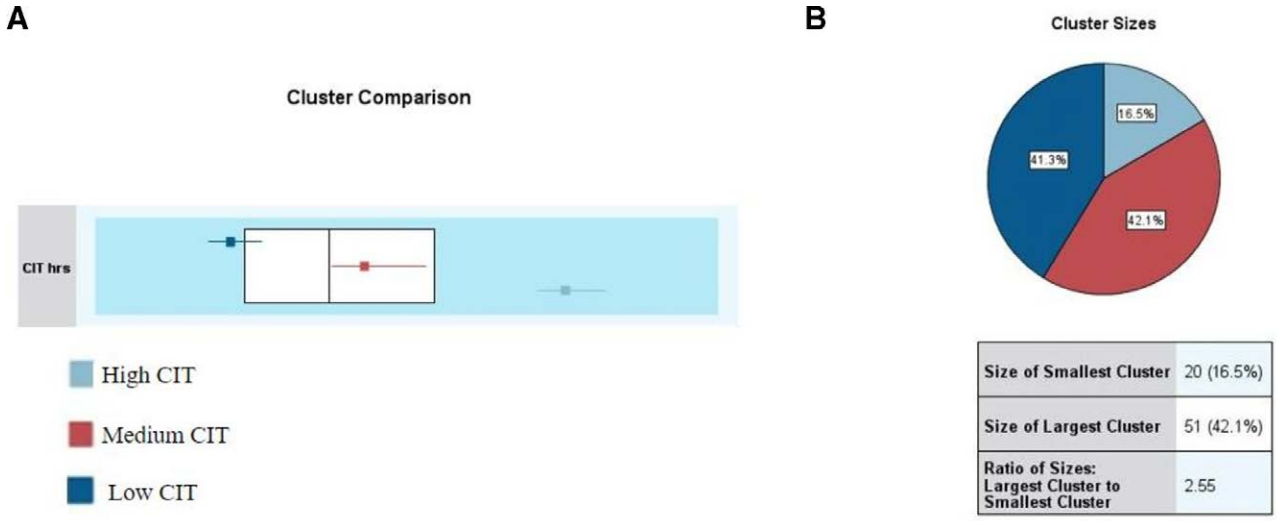

FIGURE 2. Cluster comparison and analysis of the groups. A, Comparison of the groups: "high" CIT 22.48 h (range: 19.07–27.82 h),"medium" CIT 14.75 h (range: 12.25–19.07 h), "low" CIT 9.81 h (range: 4.8–12.25 h). B, Analysis: "high" CIT, n = 50; "medium" CIT, n = 51; "low" CIT, n = 20. Ratio to size 2.55. CIT, cold ischemia time. CIT, cold ischemia time.

survival was detected (RAKT and OKT, $r = -0.19$; $P = 0.04$ and $r = -0.25$; $P = 0.004$). In probit regression models, CIT maintained significance in the effect of DGF in both open and robotic settings, but marginal effect of CIT in RAKT was higher than in the OKT group, 0.00042 versus 0.0003 respectively.

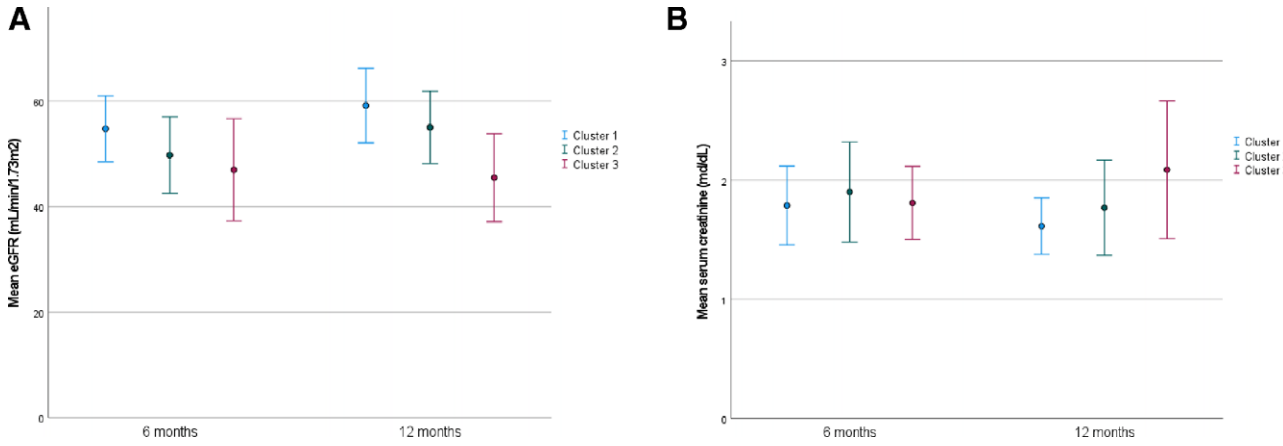

FIGURE 3. Estimated eGFR and serum creatinine estimated by clusters at 6 and 12 mo after transplant. A, eGFR. B, Serum creatinine. eGFR, estimated glomerular filtration rate.

Cluster Analysis

After the cluster analysis was performed in RAKT group for CIT, 3 groups were generated (Cluster1, n = 38; Cluster2, n = 44, Cluster3, n = 33) (Figure 1 A and B). The cluster had the following medians Cluster1 = 9.51 (1.55) h, Cluster2 = 13.63 (2.12) h, Cluster3 = 21.2 (4.79) h (Figure 2A and B). The rate of DGF was significantly higher in Cluster3 (Cluster1 versus Cluster2 versus Cluster3, 15.8% versus 34.1% versus 48.5%; $P = 0.01$). At the same time, mean estimated glomerular filtration rate at 12-mo follow-up in Cluster3 was 45.5 ± 19.7 mL/min/1.73 m^2 which was significantly lower than in the other groups (Cluster1 versus Cluster2 versus Cluster3, 59.2 ± 20.5 versus 55.1 ± 21.2 versus 45.5 ± 19.7 mL/min/1.73 m^2; $P = 0.04$) (Figure 3A). No statistical difference in mean serum creatinine levels between the clusters was registered at 6- and 12-mo follow-up (Figure 3B).

Survival

At the same time, there was no statistically significant difference in 1-y death-censored graft survival between the clusters (Cluster1 versus Cluster2 versus Cluster3, 100% versus 97.7% versus 97%; $P = 0.6$).

DISCUSSION

The global prevalence of obesity is steadily rising, currently affecting more than 40% of the US population.[7] Alongside this increase, we are seeing a surge in related health issues such as metabolic syndrome and chronic kidney disease.[8] Although there is growing interest in managing obesity among patients with end-stage renal disease, and recent guidelines even suggest that transplant could offer a survival benefit for obese individuals compared with dialysis, decisions about organ acceptance, and transplantation largely hinge on subjective criteria.[9,10]

Robotic kidney transplant is proven to be an effective and safe approach to this particular category of patients who otherwise would be denied access to a kidney transplant, not only in living donor setting but also with deceased donors.

Our group recently published a cohort of 93 obese patients underwent robotic kidney transplant from deceased donor demonstrating that RAKT for obese patients using grafts from deceased donors yields similar graft and patient survival outcomes as those in the United Network for Organ Sharing national data. Yet, in our findings, a CIT exceeding 14.5 h was significantly linked to DGF with a hazard ratio of 7.218 (95% confidence interval, 1.039-50.156; $P = .04$).[2]

Because of the time-sensitive nature of robotic transplant, the effect of CIT is vital to study to ensure patient safety and long-term graft survival.

CIT is widely acknowledged within the renal transplantation field as a potential risk factor. However, there is a lack of consensus regarding the modality CIT may influence graft prognosis, nor is there an established threshold that dictates the advisability of proceeding with transplantation. This has become even more relevant in the context of robotic kidney transplantation from deceased donors, and, to our knowledge, this is the largest cohort reported in the literature on this specific subject.

A commonly recognized factor of adverse prognostic indicator, significantly impacting the incidence of DGF and adversely affecting the long-term survival of grafts is prolonged WIT.[11] However, within our cohort, a statistically significant correlation between prolonged WIT and the incidence of DGF was not observed.

On the other hand, in our population, prolonged CIT was identified as a primary determinant influencing the onset of DGF. In the context of RAKT, critical factors contributing to DGF included not only CIT, but also the age of the donor, the KDPI, and the duration of the surgical procedure. In contrast, for OKT, CIT and DCD emerged as the predominant elements associated with an increased incidence of DGF.[2]

By examining Tables 1 and 2, a profile emerges characterizing the typical donor and recipient for both RAKT and OKT procedures. The average recipient in the RAKT group was younger, had a higher weight and BMI, and was less likely to have a history of diabetes and heart disease. Conversely, the average OKT recipient was older, weighed less, and had a greater prevalence of diabetes and heart disease. As for the donors, the average RAKT donor was younger with a lower KDPI, although this difference was not pronounced enough to influence graft survival. This observation aligns with the rigorous patient selection criteria implemented at our center. Specifically, we identify age >65 y and significant

cardiovascular comorbidities, including heart failure and calcified iliac vessels, as contraindications for robotic transplantation. Conversely, a BMI exceeding 30 kg/m^2 remains a criterion for indicating recipients as suitable candidates for this procedure.

When comparing DGF occurrences between patients undergoing RAKT and those undergoing OKT, the DGF rates for the RAKT group were marginally higher than the OKT group. Probit analysis revealed that CIT significantly impacted DGF in both RAKT and OKT procedures, with the relationship being more pronounced in the OKT group, showing that when increasing CIT by a minute, the chances of DGF increased by 0.03% in the OKT group and 0.04% in RAKT. Nonetheless, this variation was not statistically significant. A recent study has also delineated a proportional correlation between CIT and graft failure, suggesting an incremental risk of the latter commensurate with each additional hour of CIT.[12]

The rationale for stratifying into 3 uniform clusters based on CIT duration—categorized as "short" (average 9.3 ho), "intermediate" (average 13.6 h), and "prolonged" (average 20.5 h)—is articulated in an effort to ascertain a threshold past, which the likelihood of DGF supersedes the advantages of conducting a robotic transplant.

Kayler et al[13] reported that DGF was considerably more probable among patient who underwent OKT with extended CIT, particularly noting markedly elevated incidence when CIT was ≥15 h. However, they observed that the overall incidence of graft loss did not differ significantly between recipients with longer CIT compared with those experiencing shorter CIT.[13]

This observation aligns with the results obtained in our investigation. Specifically, our data suggest that patients who received RAKT experienced a higher incidence of DGF with increased CIT, though this did not significantly affect survival and graft loss rates. At the 12-mo follow-up, renal function was notably diminished in the cluster with prolonged CIT compared with the other 2 groups. However, no significant variations in average serum creatinine levels were observed between the clusters at the 6- and 12-mo follow-ups.

Moreover, our data revealed 1-y survival rates between 97% and 100% across all three clusters, with no discernible statistical difference.

Peters-Sengers et al[14] presented interesting findings on the relationship between CIT and DGF. In their cohort, they observed that when CIT exceeded 12 h, there was an increased risk of graft failure in kidneys from DCD compared with those from DBD. The risk of graft failure rose progressively with longer CIT and for CIT exceeding 24 h, the 5-y survival rate with a functioning graft was 58.8% for recipients of DCD kidneys, in contrast to 72.4% for recipients of DBD kidneys. However, if CIT remained <18 h, there was no significant difference in graft failure rates between DCD and DBD donor kidneys.[14]

CONCLUSION

The results from our study demonstrate that the effect of CIT on DGF in settings of robotic kidney transplantation follows a similar pattern as in traditional OKT. Therefore, based on our favorable results, the robotic approach should be encouraged even in setting of deceased donation. However, a prudent approach is warranted, particularly when the CIT) surpasses 20 h.

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