Effect of Cold Ischemia Time on Kidney Graft Function and Survival: Differences Between Paired Kidney Transplants From the Same Donor

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ABSTRACT

Introduction. Kidney transplantation procedures commonly result in a cold ischemia time (CIT) gap when both kidney grafts are implanted in the same center. Owing to logistics, the procedure is usually consecutive, first accomplishing one surgery and then the other. CIT constitutes an independent risk factor for the development of delayed graft function (DGF) in kidney transplants. The effect that CIT exerts on graft and patient survival is still unclear. This study evaluates the relation of CIT and transplant outcomes by comparing paired kidney transplants in terms of survival and graft function.

Methods. We accomplished a retrospective analysis of 402 kidney transplants performed in our center between 2000 and 2017. We selected all transplants where both organs from the same donor were implanted at our hospital, establishing 2 study groups (group 1: first graft implanted and group 2: second graft implanted) to compare by paired data statistical methods.

Results. We found an increase in the incidence of DGF in group 2 (42% vs 28.8%; $P < .05$). Group 2 had significantly worse graft function on day 5 posttransplant (4.7 ± 2.88 vs 3.86 ± 2.8 mg/dL of serum creatinine; $P < .05$). No significant differences in graft function were found on days 30 and 90 posttransplant. We didn't find any difference in graft survival between both groups. Length of hospitalization stay (17.6 days [± 13] vs 21.6 days [± 17]) and hemodialysis sessions (mean of 2.8 [± 2] vs 3.6 [± 2.2]) were higher in group 2.

Conclusion. CIT acts as an independent risk factor for the development of DGF in kidney transplantation. CIT had no isolated effect on graft survival.

THERE is actually no agreement on the effect that cold ischemia time (CIT) exerts directly on patient and graft survival after kidney transplantation [1–3]. Recent data suggest that CIT could act as an independent risk factor for both patient and organ survival [4]; nevertheless, findings in this work are subject to not considering delayed graft function (DGF) as a confounding factor but a part of the causal pathway [4,5]. Either way, CIT has been clearly related as an independent risk factor for DGF in kidney transplantation [6,7]. Moreover, DGF is consistently related with worse kidney transplant outcomes in terms of graft survival or function and patient survival [3,8]. Furthermore, DGF and CIT are related as independent risk factors with an increment in transplant related costs and readmissions [9].

In the common transplant process of organ retrieval and transplantation, kidneys pairs from the same donor usually have a disparity on their CIT. This is explained because, owing to logistic reasons, the procedure is usually consecutive, first accomplishing one of the kidney transplant surgeries and then the other one [10,11].

The aim of this study is to determinate if CIT is related to worse transplant outcomes by comparing paired kidney transplants in terms of survival and graft function.

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Table 1. Demographic Characteristics of Both Groups

	Group 1	Group 2	*P*
Age (x years ±SD)	50.53 ± 13.2	51.5 ± 12.1	ns
Sex F/M	59/142	57/144	ns
Transplant Number			ns
First Tx	148	129	ns
Second Tx	42	52	ns
Third Tx	10	16	ns
Fourth Tx	1	4	ns
HLA Mismatch (X ± SD)	3.8 ± 1.2	4 ± 1.1	ns
CKD Etiology			ns
GM	73	77	ns
DN	29	24	ns
Vascular	23	27	ns
Genetic	28	25	ns
Other/Unknown	48	48	ns
CIT (x hours ± SD)	16.7 ± 5.9	22 ± 4.6	< .05

CIT, cold ischemia time; CKD, chronic kidney disease; DN, diabetic neuropathy; GM, glomerular disease; HLA, human leukocyte antigen; ns, not significant; SD, standard deviation.

MATERIALS AND METHOD

We retrospectively analyzed 402 kidney transplants (201 donors) in which both kidneys from the same donor were transplanted at our center between 2000 and 2017. Patients with transplants performed in the first place formed one group to compare (group 1), and second-place transplants were included in the other group to compare (group 2). Data from each patient was extracted from our database system, including age; sex; HLA mismatch; previous transplants; CKD etiology; CIT; length of hospitalization stay; number of hemodialysis sessions during hospitalization; days of transplant survival; graft failure date; and serum creatinine at baseline, 5 days, 30 days, and 90 days. DGF was defined as a need for hemodialysis session within the first week after transplant.

Statistical analysis was performed with SPSS 22.0 IBM software; variables were assessed with a paired data comparison test. Categorical parameters were compared by McNemar's test, and continuous variables were compared with Wilcoxon's signed-rank test. Graft survival was approached with Kaplan-Meier curves and compared using the long-rank test.

RESULTS

Both groups were homogenous. There were no statistical differences between group 1 and 2 with respect to age, sex, HLA mismatch, number of previous transplants, or CKD etiology (Table 1). Median cold ischemia time was 16.7 hours (± 5.9) in group 1 and 22.0 hours (± 4.6) in group 2 ($P < .005$). Incidence of DGF was 28.8% in group 1 compared to 42% in group 2, which is statistically significant ($P < .05$). Median serum creatinine was 3.86 (± 2.8) vs 4.7 (± 2.88) on day 5 ($P < .05$), 2.09 (± 1.86) vs 2.36 (± 1.86) on day 30 (pNS) and 2.02 (± 1.59) vs 2.16 mg/dL (± 1.5) on day 90 (pNS) respectively. Length of hospitalization stay was 17.6 days (± 13) in group 1 vs 21.6 days (± 17) in group 2, this difference being statistically significant ($P < .005$). Patients in group 1 needed a mean of 2.8 (± 2) hemodialysis sessions and 3.6 (± 2.2) in group 2 ($P < .005$). No significant differences were found in graft survival.

DISCUSSION

Cold ischemia time is still a central issue in kidney transplantation. Actually, all transplantation teams aim to reduce this CIT in order to improve transplantation outcomes. It is yet unclear the pathological implication of CIT in graft and patient survival. Notwithstanding, the relationship between CIT and DGF is better established. According to recent findings [1,3,10], we found in our study that incidence of DGF increases as cold ischemia time is prolonged. We found that grafts transplanted in second place had more incidence of DGF than their graft mates. Therefore, CIT appears to be a risk factor for the development of DGF. Conversely, in our study we didn't find significant differences on graft survival. This finding may show a poor partaking of CIT in long-term graft losses. Thus, Kayler et al [3], in a longer cohort, paired kidney organ and stratified CIT analysis and did not find any differences in graft loss either. We found in our analysis that second-place procedure transplantation, therefore longer CIT and more DGF incidence, had a longer length of hospitalization stay. This means that longer CIT could be traduced in an increase in transplant related costs, as Serrano et al [9] recently found. Probably owing to the higher incidence of DGF and worse initial graft function, patients transplanted on the second place needed more hemodialysis sessions than those transplanted first. Hence, because of this issue, CIT could increase spending even more.

CONCLUSION

CIT is an independent risk factor for the development of DGF. Longer DGF incidence could entail an increase in spending on transplant-related cost owing to a longer length of hospitalization stay and an increment of hemodialysis requirements. CIT has no implication in kidney transplantation graft survival.

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