Comparison Between Kidney Transplantation After Circulatory Death and After Brain Death: A Monocentric Retrospective Study After 1 Year of Follow-up

Giacomo Mori[a,*], Andrea Solazzo[a], Laura Tonelli[a], Francesca Facchini[a], Francesco Fontana[a], Gaetano Alfano[a], Stefano Baroni[b], and Gianni Cappelli[a]

[a]Surgical, Medical, and Dental Department of Morphological Sciences, Section of Nephrology, University Hospital of Modena, Modena, Italy; and [b]Intensive Care Unit, Civil Hospital of Baggiovara, Modena, Italy

ABSTRACT

Background. Donation after circulatory death (DCD) is a solid resource to widen the kidney donor pool. Italian activity has grown in the last years with encouraging results. Our center has been active in DCD kidney transplantation (KTX) since November 2017, providing 22.5% of Italian DCD donations in 2018. We present a single-center retrospective analysis after a 1-year follow-up comparing DCD and donation after brain death (DBD) KTX outcomes.

Methods. DCD (controlled only) and DBD KTX performed in our center from November 2017 to December 2018 were considered. All DCDs underwent in situ normothermic perfusion with extracorporeal membrane oxygenation, ex situ hypothermic oxygenated perfusion, and renal biopsy prior to allocation.

We considered features of donors and recipients, immunosuppressive regimen, delayed graft function (DGF), primary nonfunction (PNF), graft and patient survival (Kaplan-Meier), creatinine, and estimated glomerular filtration rate at 1 year. Mean comparison with a Student t test and with χ^2 test for frequencies were elaborated.

Results. Twenty-eight DBD, 18 double (64.3%) and 10 single (35.7%), were performed; 7 DCD, 3 double (42.8%) and 4 single (57.2%), were performed. By comparing single and double KTX, no statistically significant difference was found. We recorded 7 DGFs (25%) in DBD and 1 (14.3%) in the DCD group ($P > .99$) and no PNF. No graft was lost during the first year. One-year estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration) was, respectively, 62.7 ± 25.3 and 54.71 ± 14.66 mL/min ($P = .25$). DBD patient survival rate was 92.8%, DCD was 100%, and Kaplan-Meier was not statistically significant ($P = .72$).

Conclusions. Controlled DCD is a valid resource for KTX, with similar outcomes to DBD. A multidisciplinary donor evaluation, combining clinical, perfusion, and histologic data in the allocation process, allows excellent results.

KIDNEY transplantation (KTX) is the best therapy for end-stage renal disease [1]. However, the number of grafts procured per year is still insufficient to satisfy the general demand, causing long waiting list times [2]. As a consequence, donation after circulatory death (DCD) is spreading across Europe due to donation after brain death (DBD) organ shortage. Spain is the benchmark country with 18.4 pmp DCD kidney transplants (KTX) in 2018 [3]. Italian experience in DCD is growing, after an initial reluctance related to cardiac death declaration legislation, which requires a minimum 20 minutes asystolia. DCD KTX nearly

*Address correspondence to Giacomo Mori, University Hospital do Modena, Via del Pozzo 71 41124, Modena, Italy. Tel: +39 059 422 567; +39 333 4814724; Fax +39 059 422 4533. E-mail: mori.giacomo@aou.it

0041-1345/20
https://doi.org/10.1016/j.transproceed.2020.02.043

doubled last year, reaching 1.1 pmp (n = 63; 42.1% Maastricht II, 56.1% Maastricht III, and 1.8% Maastricht 4) in 2018, with 22.5% of donors procured at our center [4]. Our DCD KTX protocol has been active since November 2017, with promising results [5]. According to the Emilia Romagna regional policy, only controlled DCD (cDCD) are considered, after informed consent and futile therapy withdrawal in ICU patients (Maastricht class III) [6,7]. cDCD allows shorter warm ischemia time when compared to donors with sudden cardiac arrest (uncontrolled DCD), leading to significantly better outcomes. We present a single-center retrospective analysis after 1 year of follow-up, comparing results of KTX from DCD and DBD.

MATERIALS AND METHODS

We compared all DCD and DBD KTX performed in the Nephrology Unit of the University Hospital of Modena, Italy, from November 2017 to December 2018. We excluded living donor transplantation and combined liver–kidney transplantation. According to Italian law, a minimum of 20 minutes of isoelectric electrocardiogram must be recorded before cardiac death declaration. In this protocol, only cDCD are considered. Every DCD underwent in situ normothermic regional perfusion (extracorporeal membrane oxygenation), followed by ex situ hypothermic oxygenated perfusion (HOPE) by kidney assist to improve graft preservation. Kidney biopsy was always performed to rule out irreversible acute damage (eg, thrombotic microangiopathy) and as allocation criteria, according to Karpinski score (single KTX under 4 + 4, discard over 6 + 6, double KTX in between). A maximum age of 70 years was accepted for DCD donors. In DBD, we performed kidney biopsy only in expanded criteria donors (ECD), defined either as subjects older than 65 years without comorbidities or younger but with comorbidities, such as hypertension, cerebral stroke, or high creatinine level (above 1.5 mg/dL). We report induction and maintenance immunosuppressive therapy as well as donor/recipient clinical and immunologic characteristics (age, cause of death, ischemia time, HLA match; Table 1). KTX outcomes were: delayed graft function (DGF), defined as the need for dialysis after KTX; primary nonfunction (PNF); kidney function at discharge, at 1 month, and at 1 year after KTX; grafts; and patients survival. Descriptive statistics are reported as mean and standard deviation for continuous variables and frequency for categorical variables. A comparison between data from DCD and DBD was performed with a Student *t* test and with χ^2 test, and survival analysis was performed according to Kaplan-Meier. A *P* lower than .05 was considered significant.

RESULTS

A total of 28 DBD KTX, 18 double (64.3%) and 10 single (35.7%), were observed; 7 DCD KTX, 3 double (42.8%) and 4 single (57.2%), were observed during the study. DBD and DCD donors and recipients were homogeneous in characteristics: mean age of DBD donors 59.8 ± 23.12 years

Table 1. Population Characteristics

	DBD Donor	DCD Donor	DBD Recipient	DCD Recipient
Cause of Death				
Head trauma	4	1		
Ischemic stroke	3	1		
Cerebral hemorrhage	14	2		
Postanoxic encephalopathy	4	3		
Mean age at Tx (years)	59.8 ± 23.12	58.7 ± 7.2	58.6 ± 16.6	57.4 ± 4.2
Waiting list (month)			29.7 ± 30.1	22.45 ± 41.23
Karpinski (mean)				
Double: right kidney	3.8 ± 0.9	4.6 ± 0.5		
Double: left kidney	4.4 ± 1.1	5 ± 1		
Single	2.1 ± 0.7	1.6 ± 0.5		
Cold ischemia time mean (hh:mm)				
Double: right kidney			13:00 ± 02:47	12:30 ± 00:44
Double: left kidney			13:30 ± 02:56	13:51 ± 01:06
single			12:32 ± 03:29	09:46 ± 02:40
HLA mismatch			4 ± 0.78	4.1 ± 0.98
Mean creatinine (mg/dL)				
First month			1.61 ± 1.11	1.60 ± 0.60
Third month			1.52 ± 0.62	1.41 ± 0.32
First year			1.58 ± 0.91	1.58 ± 0.90
Mean eGFR mL/min (CKD-EPI)				
First month			61 ± 25.75	54.14 ± 23.74
Third month			61.21 ± 26.90	56 ± 15.72
First year			60.26 ± 26.56	51.85 ± 12.47
DGF, n (%)			7(25%)	1 (14.3%)
PNF			0	0
Death (n)			2	0

Abbreviations: CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; DBD, donation after brain death; DCD, donation after circulatory death; DGF, delayed graft function; eGFR, estimated glomerular filtration rate; PNF, primary nonfunction; Tx, transplantation.

and DBD recipients 58.6 ± 16.6 years; DCD donors 58.7 ± 7.2 years and DCD recipients 57.4 ± 4.2 years; graft cold ischemia time DBD (double right/left 13:00 ± 02:47/13:30 ± 02:56; single 12:32 ± 03:29) and DCD (double right/left 12:30 ± 00:44/13:51 ± 01:06; single 09:46 ± 02:40); donor/recipient HLA mismatch DBD 4 ± 0.78, DCD 4.1 ± 0.98. All DCD donors and 64.3% of DBD donors underwent kidney biopsy (see Table 1 for Karpinski score). All DCD recipients received induction immunosuppression with antithymocyte immunoglobulins (aTG). In DBD KTX, antithymocyte immunoglobulins accounted for 50% of the patients (sensitized recipients, ECD), while anti-interleukin-2 receptor monoclonal antibodies (basiliximab) were administered to the other half (standard recipients). Maintenance immunosuppression consisted of steroids, tacrolimus, and mycophenolic acid. For DCD KTX, HOPE solution blood gases and biochemistry were monitored every 15 minutes to assess organ function. Mean lactate dehydrogenase values of 360.2 ± 363.2 IU/L at the beginning and 455.6 ± 233.1 IU/L at the end of perfusion were detected on the HOPE solution; lactates were 0.7 ± 0.2 mmol/L initially and 0.8 ± 0.4 mmol/L at the end of perfusion. No graft was discarded after extracorporeal membrane oxygenation and HOPE. By comparing the results from DBD and DCD KTX, no statistically significant difference was found. We recorded 7 DGFs (25%) in the DBD KTX and 1 (14.3%) in the DCD ($P > .99$). There was no PNFs in either group. Hospital stay was similar in days: 18 ± 15 DBD and 14.6 ± 0.47 DCD ($P = .45$). After 1 year of follow-up, mean serum creatinine resulted in 1.54 ± 0.79 mg/dL in DBD and 1.43 ± 0.31 mg/dL in DCD ($P = .3$); estimated glomerular filtration rate (calculated with Chronic Kidney Disease Epidemiology Collaboration formula) was, respectively, 62.7 ± 25.3 and 54.71 ± 14.66 mL/min ($P = .25$). We stratified both groups in single and double KTX, and still no statistical difference resulted. Survival analysis did not show any death-censored graft loss in the first year, although 2 DBD recipients died (1 circulatory arrest, 1 sepsis). Thus, patient survival was 92.8% for the DBD group and 100% for the DCD group ($P = .72$).

DISCUSSION

Our experience describes comparable results for DBD and cDCD KTX. No statistically significant difference was demonstrated in terms of renal function or survival rate after 1 year of follow-up. DGF and PNF rates were excellent, as was estimated glomerular filtration rate. A multidisciplinary evaluation of donors, short ischemia times (thanks to the Emilia Romagna organs allocation network), and the use of the Karpinski score granted outcomes not inferior to DBD KTX outcomes. Lactate dehydrogenase and lactic acid measurements during machine perfusion did not raise any concern on graft quality; thus, no graft was discarded after HOPE. The single transplantation rate was not reduced by DCD donation, therefore highlighting the screened organs' quality and the regional procurement system's efficiency. Double KTX seems a solid strategy to ensure good results when using ECD. The satisfying results found in the DCD group are partly due to slightly inferior mean age of donors and standard deviation (although not statistically significant when compared to DBD) and the uncontrolled DCD exclusion from our protocol. A small sample size is the main limit of this study.

CONCLUSIONS

No significant difference in terms of outcomes was described between cDCD and DBD KTX after 1 year of follow-up. cDCD was confirmed to be a viable resource to expand the donor pool. Optimal results can be reached with a multidisciplinary donor evaluation, combining clinical, perfusion, and histologic data in the allocation process. Further experience is needed to support ECD DCD donation.

REFERENCES

[1] Tonelli M, Wiebe N, Knoll G, et al. Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. Am J Transplant 2011;11:2093–109.

[2] Summers DM, Counter C, Johnson RJ, Murphy PG, Neuberger JM, Bradley JA. Is the increase in DCD organ donors in the United Kingdom contributing to a decline in DBD donors? Transplantation 2010;90:1506–10.

[3] Domìnguez-Gil B, Matesanz R. International figures on ogan, tissue & hematopoietic stem cell donation & transplantation activities. Documents produced by the council of Europe European Committee (partial agreement) on organ transplantation (CD-P-TO).Year 2017. Newsletter Transplant 2018;23.

[4] Domìnguez-Gil B. International figures on ogan, tissue & hematopoietic stem cell donation & transplantation activities. Documents produced by the council of Europe European Committee (partial agreement) on organ transplantation (CD-P-TO). Year 2018. Newsletter Transplant 2019;24.

[5] Mori G, Cerami C, Facchini F, et al. Kidney transplantation from circulatory death donors: monocentric experience. Transplant Proc 2019;51:2865–7.

[6] Kootstra G, van Heurn E. Non-heartbeating donation of kidneys for transplantation. Nat Clin Pract Nephrol 2007;3:154–63.

[7] Thuong M, Ruiz A, Evrard P, et al. New classification of donation after circulatory death donors definitions and terminology. Transpl Int 2016;29:749–59.