Kidney Transplantation From Circulatory Death Donors: Monocentric Experience

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ABSTRACT

Background. Donation after circulatory death (DCD) is an accepted strategy to widen organ procurement worldwide. Authorized centers in Italy are spreading, increasing kidney transplantation (KTX) from DCD donors (40 in 2017 vs 24 in 2016). In this study, we describe DCD KTX activity at the University of Modena and Reggio Emilia (Modena, Italy) since its beginning in November 2017.

Methods. We retrospectively studied DCD KTX performed in our center from November 2017 to June 2018. We considered donor characteristics (age, sex, cause of death) and recipient clinical data (length of hospital stay, serum creatinine, estimated glomerular filtration rate, delayed graft function [DGF]), primary nonfunction [PNF], HLA match). All the grafts underwent in situ normothermic (ExtraCorporeal Membrane Oxygenation-ECMO) and ex situ hypothermic oxygenated perfusion (HOPE) with Kidney Assist machines. We monitored ex situ perfusion solution biochemical (lactate dehydrogenase [LDH] and lactate) and dynamic (resistance and flow) parameters. A kidney biopsy was performed for allocation strategy according to Karpinski score.

Results. We performed 6 kidney transplants (3 single and 3 double); the mean recipient (57.5 ± 4.9) and donor age (57.3 ± 7.5) were similar. Mean ECMO duration was 3 h 27 ± 57 min, HOPE was 4 h 47 min ± 119 min, lactate sample values (collected every 15 minutes from the beginning of perfusion) were always lower than 1.6 mmol/L, and LDH maximum value was 400 UI/L. Median cold ischemia time was 11 h 18 min. Mean Karpinski score was 3.6; mean HLA match 1.7. We experienced 1 DGF (16.6%), no PNF, with a mean hospital stay of 14.6 days, mean creatinine at hospital discharge 2 ± 1.04 mg/dL), and mean eGFR 53.8 ± 27.3 mL/min); at 1 month, mean creatinine and eGFR were 2 ± 1.34 mg/dL and 59.8 ± 24.5 mL/min, respectively.

Conclusions. DCD is a promising resource for increasing organ donation. The Emilia Romagna regional organization allowed short ischemia times, with solid KTX outcomes, supporting further development of this program.

KIDNEY transplantation (KTX) is the best treatment for end-stage renal disease, but the shortage of deceased donors can cause long waiting list times [1–3]. Donation after circulatory death (DCD) is a recognized source of organs worldwide. In Europe, the United Kingdom, the Netherlands,

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and Belgium have stable DCD programs, providing 25% to 30% of the overall grafts (7.0-9.5 donors/pmp in 2013) [4]. The first Italian DCD protocol was implemented in Pavia in 2009 [5]; following this example, the number of authorized centers gradually increased, with progressively higher DCD KTX year by year (24 in 2016, 40 in 2017) [6].

This promising activity is overcoming the initial reluctance to DCD donors in Italy, mainly due to the 20 minutes of asystolia prescribed by Italian law to declare cardiac death and to the concern that transplant outcomes could be poorer than donors after brain death KTX [7].

The present study reports the early experience in DCD KTX at University Hospital of Modena since its authorization in November 2017.

We applied the Emilia Romagna donation after brain death allocation policy to DCD with regional procurement for 3 transplant centers: Modena, Bologna, and Parma. Dual kidney transplantation was performed according to the Karpinski score, reaching adequate results even with expanded criteria donors.

MATERIALS AND METHODS

We describe DCD KTX activity the University Hospital of Modena from the implementation of the program in November 2017 to June 2018.

According to our protocol, every graft underwent in situ normothermic regional perfusion (ECMO), followed by ex situ hypothermic oxygenated perfusion (HOPE) by Kidney Assist, to ensure optimal graft preservation and evaluation. A kidney biopsy was performed for allocation strategy based on the Karpinski score (Single KTX up to 4-4, discarded over 6-6, double for intermediate values). Immunosuppression therapy included induction with antithymocyte globulins and maintenance with steroids, tacrolimus, and mycophenolic acid.

We evaluated clinical and immunologic characteristics of donors (age, sex, cause of death, ischemia time), recipients (age, sex, HLA match), and transplantation outcomes (delayed graft function [DGF] defined as the need for dialysis after KTX, PNF kidney function at discharge and at 1 month after KTX). Categorical variables are described as frequencies and absolute values, continuous variables as mean ± standard deviation.

RESULTS

We performed a total of 6 KTX (3 single and 3 double) from Maastricht category III DCD donors (Table 1). Time from asystole to ECMO start was 20 minutes. ECMO was established postasystole via aortic and caval cannulation and maintained for an average of 3 h 27 minutes (range, 2 h 51 min-4 h 44 min). The mean duration of HOPE was 4 h 47 min (range, 2 h 52 min-7 h 47 min), perfusion was maintained at an inferior systolic pressure of 120 mm Hg, average flow was 130 mL/min, and mean resistance was < 0.2 (Ru). Median cold ischemia time was 11 h 32 min (range, 7 h 21 min-15 h 25 min). HOPE solution blood gases and biochemistry were monitored every 15 minutes to assess organ function, and lactate sample values were always lower than1.6 mmol/L (0.5-1.6), while LDH maximum value was

Table 1. Population Characteristics

Recipient age (years mean ± SD)	57.5 ± 4.97 (n = 6)
Waiting list time (days mean ± SD)	366.94 ± 739.11
Donor age (years mean ± SD)	57.3 ± 7.53 (n = 6)
Dual kidney transplant	3/7 (42.8%)
Total Karpinski score in DKT (mean ± SD)	8.25 ± 2.87
ECMO duration (h:min mean ± SD)	3:27 ± 0:40
HOPE duration (h:min mean ± SD)	4:47 ± 1:46
Cold ischemia (h:min mean ± SD)	11:44 ± 2:36
PNF	0/6 (0%)
DGF	1/6 (16.7%)
HLA A-B-DR match (mean ± SD)	1.67 ± 1.03
Hospitalization (days mean ± SD)	14.67 ± 2.73
CKD-EPI on dismission (mL/min mean ± SD)	47.50 ± 26.40
CKD-EPI 1 month (mL/min mean ± SD)	59.8 ± 22.37
CKD-EPI 6 months (mL/min mean ± SD)	51.17 ± 13.86

CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration eGFR; DGF, delayed graft function; DKT, dual kidney transplantation; ECMO, extracorporeal membrane oxygenation; HOPE, hypothermic oxygenated perfusion; PNF, primary nonfunction; SD, standard deviation.

400 UI/L (94-391). During the study period, no organ subjected to ECMO and HOPE was discarded.

The average age of the recipient was 57.5 years while donor age was 57.3 years. The median creatinine at discharge was 2 mg/dL (range, 0.9-4.5). We experienced 1 DGF at 16.6% (1 hemodialysis session) due to iperkaliemia and no PNF. Mean hospital stay was 14.6 ± 3 days. Average Karpinski score was 3.6, average HLA match 1.7.

DISCUSSION

The preliminary results of DCD KTX program of our unit confirm satisfactory outcomes in terms of kidney function, DGF, and PNF. A null discard rate in the perfused organs suggests effective donor selection criteria and an optimal procurement organization. This was also confirmed by low ischemia times regardless of donation site.

Perfusion fluid biochemical and dynamic values did not differ substantially from case to case, placing within or close to the normal range, thus not influencing clinical decisions. Further investigation is needed to identify adequate markers of acute kidney injury during machine perfusion.

CONCLUSIONS

The DCD program is a promising resource for increasing organ donations. ECMO and HOPE, combined with clinical and histological data, allowed adequate organ evaluation and recovery. In our experience, DCD KTX outcomes are satisfactory and encourage further development of the program.

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