



Kidney Transplant from Donors after Cardiocirculatory Death: An Initial Experience of a Single Centre in Portugal

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Abstract

Introduction: Donation after Cardiocirculatory Death (DCD) is a mean of addressing the shortage with the potential to increase the number of transplantable organs. The legal and ethical basis for transplants from DCD (only type 2 Maastricht) started in Portugal in 2014 and at our center in 2017. We pretend to describe our initial experience of transplantation of organs from DCD donors.

Methods: We retrospectively reviewed the medical records of DCD donors and kidney transplant recipients that occurred in 2018 at our Centre.

Results: In 2018, 7 donors were accepted in our program for DCD. Of those 14 kidneys, 9 were transplanted in our center, 3 were transplanted at other centers and 2 were not suitable for transplant. The mean age of the donors was 48.6-years and of the recipients were 45.8-years. The causes of death were traumatic brain injury (n=1), sudden cardiac arrest (n=2), respiratory arrest (n=1) and unknown (n=1). The serum creatinine average of the donors was 1.15 mg/dL. There were 1 case of acute rejection with renal vein thrombosis and was submitted to nephrectomy. The kidney function of the others recipients at 10th month of follow-up were good with a mean serum creatinine of 1.2 mg/dL.

Conclusion: Our initial results compare positively with those from the transplantation of organs obtained from donors after brain death. DCD can be an important mean of increasing the number of organs available for transplant and its widespread implementation in Portugal should be encouraged.

Introduction

A recent global problem is the persistent shortage of organ pool for transplantation. Despite increases in kidney transplantation from Expanded Criteria Donors (ECD) and Living Related Donors (LRD) in the last decades, the supply of donor kidneys remains insufficient.

The concept of Donation after Cardiocirculatory Death (DCD) is not new. It was the only source of organs for transplantation in the 1950s and 1960s. After brain-death criteria were defined and adopted in 1968, Donation after Neurologic Death (DND) became the primary source of organs for transplant, and DCD mainly ceased, except at some European and American Transplant Centre's. Recently, there has been renewed interest in DCD as a means of addressing the inadequate supply of organs [1].

The First International Workshop on DCD held in Maastricht in 1995 described four categories of DCD, depending on the irreversible cessation of circulatory and respiratory functions. Based on the Maastricht categories, uncontrolled DCDs are Type I (dead on arrival) and Type II (unsuccessful resuscitation), while controlled DCDs are Type III (awaiting cardiac arrest) and Type IV (cardiac arrest occurring with brain death). DCD accounted for 17% of the 31,812 donors reported to the Global Observatory on Organ Donation and Transplantation in 2018. However, DCD is still practiced in a limited number of countries.

European countries that actively perform DCD differ in their protocols. The highest rate of controlled DCD is recorded in the United Kingdom, Belgium, and the Netherlands while uncontrolled DCD is mainly described in France, Latvia, and Spain [2-4]. For a long time, Portugal and 9 other countries such as Cyprus, Estonia, Luxembourg, Norway, Poland, Romania, Slovak Republic, Slovenia, and Sweden have been planning to start the DCD program [4].

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Table 1: Demographic Characteristics of Donation after Cardiac Death Donors.

Donors	Sex	Age	BMI (kg/m ²)	Medical Past History	Cause of Death	sCr (mg/dL)
1	F	35	31.2	Healthy	SCA	0.76
2	F	48	22.0	Depression	Unknown	0.86
3	M	40	23.,9	Healthy	Traumatic brain injury	0.88
4	M	63	24.2	Diabetes mellitus type 2	Medical	1.67
5	F	48	26.1	Bipolar disorder	SCA	1.36
6	M	39	24.9	Hypertension, Dyslipidemia	Respiratory arrest	1.12
7	F	68	26.7	Hypertension	MI	1.10

BMI: Body Mass Index; SCA: Sudden Cardiac Arrest; MI: Myocardial Infarction; sCr: Serum Creatine

The legal and ethical basis for transplants from DCD (only type 2 Maastricht) started in Portugal in 2014. In October 2017 this program officially began at our Department of General Surgery and Kidney Transplant Unit, at the Northern Lisbon University Hospital Centre.

In 2018 there were 28 transplants from DCD in Portugal, 1856 in Europe and 4115 in the World (those 2018 data are based on the Global Observatory on Donation and Transplantation (GODT) data, produced by the WHO-ONT collaboration).

In this article, we present our initial experience with kidney transplantation using DCD organs.

Methods

We retrospectively reviewed the medical records of DCD donors and kidney transplant recipients that occurred in 2018 at our Centre.

The acceptable criteria for DCD were as follows: a) Known cause of death, ruling out violence, b) age less than 65, c) time from cardiac arrest to Cardiopulmonary Resuscitation (CPR) less than 15 min or 30 min, if previous 15 min of Basic life support, d) donors' warm ischemia time less than 150 min, e) negative history of uncontrolled diabetes mellitus and hypertension, malignancy, renal disease, extensive trauma, systemic sepsis and no external signs of possible intravenous drug addiction to control the risk of HIV or hepatitis C or B positivity.

Medical conditions of the donor and procedures that might be related during processing of organ donation were recorded. Pre- and post-transplantation medical conditions of the recipients and their graft functions were also monitored. Routine hematological testing to screen donors for infectious disease included serology for hepatitis B and C, HIV, human T lymphocyte virus 1 and Virus 2, syphilis, West Nile virus, Epstein-Barr virus and cytomegalovirus. Routine kidney function tests were performed to assess the quality of the organ. Blood samples were also taken for ABO blood group identification, human leukocyte antigen tissue typing and crossmatching with recipient blood. Donor abdominal imaging was performed systematically before organ retrieval.

After declaration of death, all patients were submitted to Normothermic Extracorporeal Membrane Oxygenation (NECMO) to minimize the deleterious effects of the warm ischemia. Then were transferred to the operating room where it was perfused with cold preservation solution (Celsior) and stored for implantation. There is currently no clear or uniform definition of the warm ischemic interval. Various definitions have been suggested and they are based on the time which the warm ischemia is thought to start [5]. The situation becomes even more complicated when Prolonged Cardiopulmonary Resuscitation (CPR) or ECMO are installed in uncontrolled DCD [6].

In our Centre the Warm Ischemia Time (WIT) was defined as the time between the cessation of cardio-circulatory activity and the initiation of cold perfusion (WIT 1), and ischemia during implantation, from removal of the organ from ice until reperfusion (WIT 2). The Cold Ischemia Time (CIT) was defined as the time between aortic cross-clamp with cold perfusion in the donor and the removal of the organ from the ice.

Recipients were selected according to our allocation criteria. For kidney recipients, polyclonal anti-T cell antibody (Thymoglobulin; Genzyme) induction with delayed introduction of tacrolimus was used because delayed graft function was expected. Maintenance immunosuppression for kidney transplant recipients was tacrolimus based with Mycophenolate mofetil and prednisone.

The kidney transplantation was performed in the usual manner by experienced surgeons. The kidneys were transplanted to the common iliac artery and vein. The ureters were implanted in bladders using Lich-Gregoir's technique. Ultrasound-guided allograft biopsy was performed in kidney recipients with delayed graft function to rule out acute rejection.

Results

Donors and donation process

In 2018, 7 donors were accepted in our program for DCD. Of the 14 kidneys removed, 9 were transplanted in our center, 3 were transplanted at other centers and 2 were not suitable for transplant. The demographic characteristics of donors after cardiac death are summarized in Table 1.

The mean age of the donors was 48.6 (range 35 to 68) years. There were no important cardiovascular diseases on donors. The causes of death were traumatic brain injury (n=1), sudden cardiac arrest (n=2), respiratory arrest (n=1) and unknown (n=1). The serum creatinine donors average was 1.15 mg/dL (range 0.76 to 1.67). The kidneys from donor 3 were not proper for transplant.

The process of donation to transplantation timings is described in Table 2. The mean cold ischemia time was 20 (range 13 to 26) h. The mean WIT 1 was 156.5 (range 126 to 256) min, and the WIT 2 was 32 (range 28 to 39) min.

Kidney transplantation

The demographics of the 8 kidney recipients (5 men: 4 women) are shown on Table 3. The mean age was 45.8 (range 36 to 58) years. The mean time on dialysis before transplantation was 6 (range 4 to 8) years.

The mean Length of Stay (LOS) in hospital was 30 (range 20 to 65) days. There was 1 case (recipient 1) of primary non-function that

Table 2: Timings of donation process.

Donors	BLS after Arrest	Time until ALS (min)	Hospital Admission (min)	ALS time (min)	Time between Death and NECMO (min)	WIT 1 (min)
1	Yes	10	60	140	9	148
2	Yes	10	73	99	24	126
3	No	4	95	70	41	256
4	Yes	8	66	70	9	183
5	Yes	6	77	67	26	214
6	Yes	13	78	67	8	170
7	No	Immediately	At the hospital	149	8	155

BLS: Basic Life Support; ALS: Advanced Life Support; NECMO- Normothermic Extracorporeal Membrane Oxygenation; WIT: Warm Ischemia Time 1 (asystole until cold perfusion)

Table 3: Characteristics of kidney recipients and functional outcomes.

Recipients	Sex	Age	Donor	Kidney disease	Years on Dialysis	CIT (hours)	WIT 2 (min)	LOS	PO dialysis (days)	sCr (10 th month PO)
1	F	38	1	Hypertensive glomerulosclerosis	5	23.6	39	27	After 1 st day	10,87
2	F	42	2	Chronic pyelonephritis with VUR	8	22.1	31	65	1	1,20
3	M	50	2	IgA nephropathy	6	26.5	28	24	11	1,25
4	M	50	3	Chronic glomerulonephritis	7	17.4	28	20	7	1,47
5	M	41	3	Hypertensive glomerulosclerosis	8	21.9	38	22	5	1,15
6	F	58	5	Chronic glomerulonephritis	4	13.4	31	24	4	0,88
7	M	46	6	Chronic glomerulonephritis	5	15.1	23	21	18	1,30
8	F	36	6	Chronic pyelonephritis with VUR	5	19.1	34	37	0	0,99
9	M	51	7	Chronic glomerulonephritis	5	16.9	29	30	3	1,68

CIT: Cold Ischemia Time; WIT: Warm Ischemia Time 2 (ice organ removal until reperfusion); LOS: Length of Stay; PO: Postoperative; sCr: Serum Creatinine; VUR: Vesicoureteral Reflux

showed features of acute rejection with renal vein thrombosis, and was submitted to nephrectomy. This patient was on dialysis since the first postoperative day. The other patients (89%) underwent biopsy because of prolonged delayed graft function (>7 d) that showed mild to moderate acute tubular necrosis without any features of acute rejection. Seven required temporary dialysis for a mean of 6 (range 0 to 18) days after transplantation.

Other postoperative complications included 4 urinary tract infections, 2 perirenal hematomas (not requiring blood transfusion) and 2 cases of New Onset Diabetes after Transplant (NODAT).

All kidneys regained function and after 1-year follow-up, kidney function was good, with a mean serum creatinine level of 1.2 (range 0.88-1.68) mg/dL.

Discussion

Our initial experience with renal allografts from DCD donors is encouraging and similar to the recent experiences reported by other centers [1,7-13].

The 88% renal allograft survival rate is the most encouraging aspect of our experience. Although there was a higher incidence of delayed graft function, recipients had excellent 1-year renal function. They are comparable to our results with renal transplants from DND donors, as described in other centers [4,8,10,11,13]. There are reports that non-heart beating donor kidneys with delayed graft function have superior graft survival compared with conventional heart beating donor kidneys that develop delayed graft function [14].

Although delayed graft function has been associated with poorer graft survival in kidneys transplanted from DND donors, this

association is less apparent in kidneys transplanted from DCD donors [14]. The broad experience shows that the incidence of delayed graft function is more than twice as seen with DND donors but the 1-year and 3-year graft survival rates are not significantly different [14,15]. It is accepted that the higher incidence of delayed graft function is related to ischemic injury sustained during the period of warm ischemia. Thus, restriction of WIT to less than 2 h is desirable, and some centers restrict it to only 1 h [6,16,17]. We made every effort to minimize the deleterious effect of cold ischemia time to compensate the expected warm ischemic injury. As it's a crucial factor because we commit personnel, time and resources, nevertheless we need to improve our times.

Effective communication between the different teams involved (Intensive Care Unit, donor and recipient transplant teams) is mandatory. This approach requires that recipients are admitted and prepared before donor surgery. Dedicated operating room staff on standby for up to 2 h for donor finding is necessary. The availability of the operating rooms and the surgical staff to do simultaneous procedures was not possible most of the time. The second kidney transplant had more prolonged CIT because we only have one surgical team available. The logistics are a challenge, and the use of hospital resources is substantial, but they are necessary to obtain good outcomes [18]. We receive referrals from centers outside Lisbon, including regional hospitals that have no transplant programs. This collaboration brought a substantial number of donor organs that would otherwise have not been used. Donation after cardiac death is a concept that should be widely disseminated and taught in hospitals throughout Portugal to reduce the number of hemodialysis patients waiting for kidney transplantation. This type of donation can be an important means of increasing the number of organs available for

transplant, and the practice should be encouraged.

A review of the first few cases of DCD was an opportunity to learn and improve our DCD program. Organs donated from Maastricht type III donors constitute 50% of kidney transplantations in others countries, such as Belgium, the United Kingdom and Holland. The use of Maastricht type III donors implies a much less complex organizational paradigm than type II donors, and such a program can be implemented in many hospitals with scarce need for additional resources [7]. The implementation of a kidney transplant program for Maastricht type III non-heart beating donors would be another adequate alternative for increasing the number of kidney transplants, thus decreasing the waiting list time for potential recipients.

Conclusion

Donation after cardiac death can be an important means of increasing the number of organs available for transplant, and its widespread implementation in Portugal should be encouraged.

References

1. Roberto HA, Yves C, William W. Kidney and Liver Transplants from Donors After Cardiac Death: Initial Experience at The London Health Sciences Centre. *Can J Surg.* 2010;53(2):93-102.
2. Brook NR, Nicholson L. Kidney Transplantation from Non-Heart-Beating Donors. *Surg.* 2003;1(6):311-22.
3. Sánchez-Fructuoso AI, Prats D, Torrente J, Pérez-Contín MJ, Fernández C, Alvarez J, et al. Renal Transplantation from Non-Heart Beating Donors: A Promising Alternative to Enlarge the Donor Pool. *J Am Soc Nephrol.* 2000;11(2):350-8.
4. Domínguez-Gil B, Haase-Kromwijk B, Leiden VH, Neuberger J, Coene L, Morel P, et al. Current Situation of Donation after Circulatory Death in European Countries. *Transpl Int.* 2011;24(7):676-86.
5. Neyrinck A, Van Raemdonck D, Monbaliu D. Donation after Circulatory Death: Current Status. *Curr Opin Anaesthesiol.* 2013;26(3):382-90.
6. Halazun KJ, Mukhtar A, Aldouri A, Willis S, Ahmad N. Warm Ischemia in Transplantation: Search for a Consensus Definition. *Transplant Proc.* 2007;39(5):1329-31.
7. Portolés-Pérez J, Rubio-Muñoz JJ, Lafuente-Covarrubias O, Sánchez-Sobrino B, Carballido-Rodríguez J, Rodríguez-Reina G, et al. Development of a Program for Kidney Transplants Using Organs Donated from Donors Awaiting Cardiac Arrest (Type Iii Maastricht). *Nefrologia.* 2012;32(6):754-9.
8. Whiting JF, Delmonico F, Morrissey P, Basadonna G, Johnson S, Lewis WD, et al. Clinical Results of an Organ Procurement Organization Effort to Increase Utilization of Donors after Cardiac Death. *Transplantation.* 2006;81(10):1368-71.
9. Lee JH, Hong SY, Oh CK, Hong YS, Yim H. Kidney Transplantation from a Donor Following Cardiac Death Supported with Extracorporeal Membrane Oxygenation. *J Korean Med Sci.* 2012;27(2):115-9.
10. Del Río F, Andrés A, Padilla M, Sánchez-Fructuoso AI, Molina M, Ruiz Á, et al. Kidney Transplantation from Donors after Uncontrolled Circulatory Death: The Spanish Experience. *Kidney Int.* 2019;95(2):420-8.
11. Vergano M, Magavern E, Baroncelli F, Frisenda V, Fonsato A, Artusio D, et al. Making a Case for Controlled Organ Donation after Cardiac Death: The Story of Italy's First Experience. *J Crit Care.* 2017;38:129-31.
12. Singh S, Kumar S, Dasgupta S, Kenwar DB, Rathi M, Sharma A, et al. A Single-Center Experience of Kidney Transplantation from Donation after Circulatory Death: Challenges and Scope in India. *Indian J Nephrol.* 2017;27(3):205-9.
13. Xue W, Tian P, Xiang H, Ding X, Pan X, Yan H, et al. Outcomes for Primary Kidney Transplantation from Donation after Citizens' Death in China: A Single Center Experience of 367 Cases. *BMC Health Serv Res.* 2017;17(1):250.
14. Brook NR, White SA, Waller JR, Veitch PS, Nicholson ML. Non-Heart Beating Donor Kidneys with Delayed Graft Function have Superior Graft Survival Compared with Conventional Heart-Beating Donor Kidneys that Develop Delayed Graft Function. *Am J Transplant.* 2003;3(5):614-8.
15. Manara AR, Murphy PG, O'Callaghan G. Donation after Circulatory Death. *Br J Anaesth.* 2012;108(Suppl 1):i108-21.
16. Kim JM, Kim SJ, Joh JW, Kwon CH, Song S, Shin M, et al. Kidney Donation after Cardiac Death in Korea. *Transplant Proc.* 2011;43(5):1434-7.
17. Rodríguez FO, Boissier R, Budde K, Figueiredo A, Taylor CF, Hevia V, et al. European Association of Urology Guidelines on Renal Transplantation: Update 2018. *Eur Urol Focus.* 2018;4(2):208-15.
18. Saidi RF, Elias N, Kawai T, Hertl M, Farrell ML, Goes N, et al. Outcome of Kidney Transplantation using Expanded Criteria Donors and Donation after Cardiac Death Kidneys: Realities and Costs. *Am J Transplant.* 2007;7(12):2769-74.