Low-dose In Situ Perfusion With Euro-Collins Solution Is Effective for the Procurement of Marginal Kidney Grafts From Donation After Circulatory Death Donors

Tamotsu Tojimbara[a,*], Jun Yashima[a], Hiroyuki Shirai[a], Noriyuki Masaki[b], Makoto Tonsho[b], and Satoshi Teraoka[b]

[a]Department of Transplant Surgery, International University of Health and Welfare, Atami Hospital, Shizuoka, Japan; and [b]International University of Health and Welfare, Mita Hospital, Tokyo, Japan

ABSTRACT

We have adopted a modified method to resuscitate kidneys from donation after circulatory death (DCD) donors with the use of Euro-Collins (EC) solution instead of University of Wisconsin solution. This study aimed to evaluate kidney transplantation (KTx) outcomes of DCD procured with low-dose in situ perfusion using EC solution.

Patients and Methods. KTx was performed in 8 adults. Kidney grafts were procured following in situ perfusion with approximately 1 L of EC solution and preserved in the solution. The kidney donor profile index value was 88% ± 21%. The terminal creatinine level of the donors was 5.5 ± 3.4 mg/dL. Of the 8 donors, 6 experienced oligoanuria prior to graft procurement.

Results. The mean age of the recipients and the hemodialysis vintage were 50 ± 10 years and 161 ± 25 months, respectively. The warm and cold ischemic times were 8.3 ± 7.9 minutes and 8.7 ± 4.3 hours, respectively. All grafts functioned after a delayed graft function of 10.6 ± 6.9 days (2–25 days). There was neither immediate graft function nor primary nonfunction. The patient and graft survivals were both 100% with a terminal creatinine level of 1.3 ± .5 mg/dL.

Conclusions. Kidney grafts procured from DCD donors with a high kidney donor profile index value demonstrated good renal function with an excellent midterm outcome. Low-dose in situ perfusion with EC solution is effective for the procurement of marginal kidney grafts from DCD donors under optimal conditions such as a relatively shorter preservation time.

DESPITE the fact that donation after circulatory death (DCD) is a well-known option for organ transplantation, especially of the kidney, a great number of DCD kidneys are deemed unsuitable for transplantation and are thus discarded [1–3]. This is mainly attributed to inadequate perfusion during in situ flushing with preservation fluid following procurement. Furthermore, most transplant teams are reluctant to perform organ procurement due to anticipated poor outcomes. In contrast, to address the issue of chronic organ shortage, kidneys from DCD donors have been accepted as an organ resource in Japan for many years. We have consistently used kidneys from such marginal donors, particularly DCD donors with high terminal creatinine (Cr) levels [4,5]. Recently, we have adopted a modified method to resuscitate DCD kidneys using Euro-Collins (EC) solution instead of University of Wisconsin (UW) solution. In this study, we evaluated kidney transplantation (KTx) outcomes of DCD kidneys procured through low-dose in situ perfusion using EC solution.

PATIENTS AND METHODS

This study was conducted in accordance with the principles of the Declarations of Helsinki and Istanbul. From September 2008 to

*Address correspondence to Tamotsu Tojimbara, MD, PhD, Department of Transplant Surgery, International University of Health and Welfare, Atami Hospital, 13-1 Higashikaigan-cho, Atami City, Shizuoka 413-0012, Japan. Tel: +81-557-81-9171; Fax: +81-557-83-6632. E-mail: tojimbara@iuhw.ac.jp

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230 Park Avenue, New York, NY 10169

October 2017, a total of 8 consecutive patients underwent KTx from DCD donors at the International University of Health and Welfare, Atami Hospital. Kidney grafts were procured with a modified method using EC solution. Procurement methods for kidney grafts from DCD donors have been reported previously [4,5]. In brief, after family authorization was obtained, prearrest cannulation was performed by inserting a double-balloon triple-lumen catheter (Create Medic Co, Yokohama, Japan) into the aorta via the femoral artery prior to cardiac arrest. In cases where prearrest cannulation was not performed, a double-balloon catheter was inserted directly into the aorta immediately after laparotomy. Regional in situ perfusion was performed by flushing EC solution through the double-balloon catheter following blood drainage via the femoral vein. The inferior vena cava in the thoracic cavity was incised and opened for additional venous drainage after laparotomy. The total amount of EC solution for flushing was approximately 1–1.5 L without any previous flushing (eg, lactated Ringer's solution). The kidneys were retrieved en bloc and each kidney was additionally perfused with a small amount of EC solution (less than 100 mL) on the back table. The preservation method employed was cold storage in all cases.

All donors were categorized as either III or IV according to Maastricht classification [6]. The causes of donor death were as follows: cerebrovascular accident/stroke (3 donors), anoxia (3 donors), and head trauma (2 donors). The mean kidney donor risk index and kidney donor profile index were 1.91 ± .63 and 88% ± 21%, respectively [1]. The mean terminal Cr level of the donors was 5.5 ± 3.4 mg/dL, whereas the mean Cr levels on admission was .8 ± .2 mg/dL (Table 1). Of the 8 donors, 6 experienced oligoanuria for 1–5 days prior to graft procurement.

All recipients underwent tacrolimus-based immunosuppression with mycophenolate mofetil. Basiliximab was used for induction therapy. Methylprednisolone was administered intravenously at 250 mg on the day of surgery and then tapered until discontinuation on postoperative day 14, in accordance with our protocol. Recipients were followed up for a mean period of 60 ± 46 months after surgery (11–118 mo).

RESULTS

In 6 of the 8 donors, prearrest cannulation was performed with family authorization. The 2 other donors did not undergo prearrest cannulation due to severe stenosis in the iliac artery and family's being against the procedure, respectively.

The parameters and outcomes among donors and recipients are summarized in Table 1. The mean age of the recipients and hemodialysis vintage were 50 ± 10 years and 161 ± 25 months, respectively. The mean HLA AB and DR mismatches were 1.75 ± .89 and .63 ± .52, respectively. The mean warm and cold ischemic times were 8.3 ± 7.9 minutes and 8.7 ± 4.3 hours, respectively. Furthermore, all grafts functioned after a delayed graft function of 10.6 ± 6.9 days. There was neither immediate graft function nor primary nonfunction. Patient and graft survival rates were both 100%. The lowest Cr levels during the study period and the last Cr levels were 1.2 ± .4 mg/dL and 1.3 ± .5 mg/dL, respectively. Changes in serum Cr levels by year after kidney transplantation are shown in Figure 1. In all of the 8 recipients, no biopsy-confirmed rejection was observed.

Table 1. Parameters and Outcomes Among Donors and Recipients (n = 8)

Characteristics	Values
Donor age (y)	53 ± 17 (27–69)
Donor sex (M/F)	5/3
Cannulation (Y/N)	6/2
Ventilator off (Y/N)	0/8
Cr levels on admission (mg/dL)	.8 ± .2 (.6–1.0)
Terminal Cr levels (mg/dL)	5.5 ± 3.4 (.6–11.2)
SCD/ECD	2/6
KDRI	1.91 ± .63 (1.00–2.64)
KDPI (%)	88 ± 21 (51–100)
WIT (min)	8.3 ± 7.9 (1–24)
TIT (h)	8.7 ± 4.3 (4.8–17.3)
Recipient age (y)	50 ± 10 (37–63)
Recipient sex (M/F)	5/3
HLA-AB mismatch	1.75 ± .89 (0-z–3)
HLA-DR mismatch	.63 ± .52 (0–1)
Pretransplant hemodialysis vintage (mo)	161 ± 25 (33–200)
Lowest Cr levels (mg/dL)	1.2 ± .4 (.7–1.7)
Last Cr levels (mg/dL)	1.3 ± .5 (.8–2.2)
Graft survivals (%)	
1 year	100
5 years	100

Abbreviations: Cr, creatinine; ECD, expanded criteria donor; KDPI, kidney donor profile index; KDRI, kidney donor risk index; SCD, standard criteria donor; TIT, total ischemic time; WIT, warm ischemic time.

DISCUSSION

In most countries, donation after brain death (DBD) donors are the most common source of organs for transplantation. However, the demand for donor kidneys cannot be met without a new source of donor organs. Recently, there has been a renewed interest in the use of kidney grafts from DCD donors, even in the United States, where DBD donors are the most common source of organs for transplantation [1–3]. Some large cohort studies have shown that the long-term graft and patient survival rates of kidneys from DCD donors are comparable with those of kidneys from DBD donors [2,7]. In Japan, donor shortage has led to the more

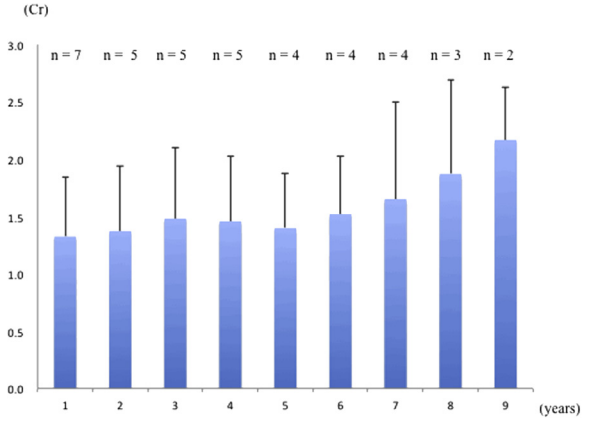

Fig 1. Changes in serum Cr levels after kidney transplantation. Values presented in mg/dL, mean ± SD.

frequent use of kidneys from marginal donors, such as extended criteria donors (ECD) and DCD donors with high terminal Cr levels. We have reported satisfactory long-term outcomes in recipients of kidney grafts procured from DCD donors mostly using UW solution [4,5].

UW solution is without a doubt one of the major contributions of clinical organ preservation for transplantation [8]. In a practical setting, however, UW solution is not always an ideal flushing and preservation solution for kidney procurement because of its shorter storage period (shelf life) and low availability, particularly in low-volume institutes where cadaveric KTx is performed at best once a year. The cost of EC solution is from one-fifth to one-tenth that of the other solutions. Although EC solution is rarely used during multi-organ procurement because of its glucose-related disadvantage, it contributes to the safe preservation of kidneys from DBD donors for up to 50 hours [8–10]. EC solution was able to protect the kidneys from swelling and ionic changes during long preservation periods in experimental DBD models. However, the actual preservation time using EC solution is not fully clarified in ECD and/or DCD donors. Summers et al suggested that DCD kidneys tolerate cold storage less well than DBD kidneys [7]. In this study, we used EC solution instead of UW solution at a relatively shorter preservation time with 8.7 ± 4.3 hours of cold ischemic time. The superiority of UW solution to EC solution is more pronounced with a longer cold storage time. In other words, it is likely that, similar to UW solution, EC solution may be more effective under optimal conditions such as a shorter preservation time. In this study, low-dose in situ perfusion with approximately 1–1.5 L of EC solution through the double-balloon triple-lumen catheter was adopted, whereas the manufacturer's recommendation is 3–4 L. Perfusion with large volumes of EC solution may cause high vascular resistance and thus hamper optimal perfusion because of its high potassium concentration (115 mmol/L) [11]. We believe that the removal of blood from the kidney graft should be accomplished by effective venous drainage, not by washing out with a flushing solution. The flushing solution should be gently infused concurrently with blood removal by venous drainage. In addition, the low viscosity of EC solution might be advantageous for flushing marginal kidney grafts, whereas organ procurement with a high-viscosity solution such as cold UW solution could result in a flush injury. It is well known that a poorly preserved vascular endothelium may lead to various adverse effects, including vasoconstriction, platelet deposition, and thrombosis, which may ultimately result in ineffective tissue perfusion and tissue necrosis. A damaged endothelium may also expose complement receptors on the cell surface, and the subsequent binding of complement to the endothelium has been suggested to increase the risk of graft rejection [12].

In this study, kidney grafts procured from DCD donors with a high kidney donor profile index value demonstrated acceptable renal function with a good midterm outcome, although further follow-up is necessary to confirm long-term outcome.

In conclusion, low-dose in situ perfusion with EC solution is effective for the procurement of marginal kidney grafts from DCD donors under optimal conditions, such as a relatively shorter preservation time. In addition, our new method with EC solution provides a great economic advantage for transplant centers, especially among low-volume institutes that perform few DCD kidney procurement procedures.

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