



# Long-Term Outcomes in Kidney Transplantation From Expanded-Criteria Donors After Circulatory Death

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## ABSTRACT

The number of recipients waiting for a transplant is increasing. In Japan, there is more frequent use of organs from expanded-criteria donors (ECDs) after circulatory death. We retrospectively analyzed long-term outcomes of kidney transplantation (KT) from expanded-criteria donation after circulatory death (DCD). From 1995 to 2013, 97 cases of KT from DCD donors were performed in our department. Death-censored graft survival rates of ECD kidneys ( $n = 50$ ) versus standard-criteria deceased-donor (SCD) kidneys ( $n = 47$ ) for 1, 5, and 10 years after transplantation were 84.0% vs 97.9%, 74.8% vs 95.6%, and 70.2% vs 81.8%, respectively. No significant difference was found between the 2 groups ( $P = .102$ ). Kidneys from donors with a history of hypertension (HTN) and cerebrovascular events (CVE) and contribution from older donors had significantly lower 10-year graft survival rates ( $P$  values of .010, .036, and .050, respectively). Cox proportional hazard regression analyses showed donor age to be significantly associated with long-term graft survival independently from other factors. These results suggest that ECD kidneys remain an acceptable alternative to dialysis under certain conditions. Increased donor age was a significant risk factor determining long-term graft function. Moreover, comorbidities of HTN and CVE could become significant risk factors, especially in older donors.

**I**N Japan, “living” kidney transplantation (KT) has been the most popular modality of organ procurement (80%–85% of all KT), and although donation after brain death (DBD) has been increasing since the organ transplant law was revised in 2010, there were only 20 DBD cases in our center from 1995 to 2013, not nearly enough to accommodate the current organ shortage. The number of recipients waiting for a transplant is increasing, so there was more frequent use of organs from expanded-criteria deceased donors (ECDs) after circulatory death. Kidneys from an expanded donor pool have been shown to receive the benefit of extra life-years compared with patients receiving dialysis who remained on a waiting list [1,2]. Furthermore, good outcomes from ECD have recently been reported for KT, compared with those from standard-criteria deceased donors (SCDs) [3–5]. However, there is limited evidence on donation after circulatory death to analyze the impact of donor age, increased terminal creatinine levels, history of hypertension (HTN), and cerebrovascular events (CVE). To evaluate these risk factors of DCD, we retrospectively

analyzed long-term outcomes of KT from expanded-criteria DCD.

## METHODS

The study was carried out in accordance with the principles of the Helsinki Declaration. From 1996 to 2013, 97 cases of KT from DCD were performed at the Department of Surgery III in Tokyo Women's Medical University Hospital. All donors were Maastricht category grade III or IV. Procurement methods for kidney grafts from DCD have been reported previously [6,7].

## Definition of ECD and SCD

ECDs were defined as either donors aged >60 years, or aged 50–59 years with any 2 of the following criteria: history of HTN, cause of death from CVE, and terminal Cr (t-Cr) level  $\geq 1.5$  mg/dL. A donor not meeting these criteria was defined as SCD.

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### Immunosuppressive Treatment and Management

All patients were treated with cyclosporine- or tacrolimus-based immunosuppression. Since 1999, mycophenolate mofetil has been used in place of azathioprine and mizoribine. Induction therapy with basiliximab began in 2002. Methylprednisolone was administered intravenously at 250 mg on the day of surgery, and then tapered until discontinuation on postoperative day 14 if possible. Supplemental methylprednisolone was given if acute rejection was suspected clinically or diagnosed by means of biopsy [6,7].

### Definition of Immediate Graft Function, Delayed Graft Function, Primary Nonfunction, and Graft Failure

Immediate graft function (IGF) was defined as life-sustaining kidney function without dialysis for 7 days after KT. Delayed graft function (DGF) was defined as kidney function that ultimately supported the patient but necessitated post-transplantation dialysis within 7 days after KT. Primary nonfunction (PNF) was defined as failed function of the transplanted kidney which necessitated continued maintenance dialysis. And graft failure was defined as return to maintenance dialysis, and included graft loss in cases of patient death with functioning graft.

### Statistical Analyses

Values were expressed as mean  $\pm$  SD. Either the Mann-Whitney test or the chi-square test was used to compare 2 independent variables. Prevalence of biopsy-proven acute rejection (BPAP) and long-term graft and patient survivals were analyzed with the use of the Kaplan-Meier estimation and assessed with the use of the log-rank test. A *P* value of  $<.05$  was considered to indicate statistical significance.

## RESULTS

### Patient Characteristics of ECD and SCD

Table 1 presents the baseline characteristics of the ECD group ( $n = 50$ ) and the SCD group ( $n = 47$ ). There were significant differences in age, history of HTN, CVE, and t-Cr levels  $\geq 1.5$  mg/dL between the ECD group and the SCD group (*P* values of  $<.001$ ,  $<.001$ , and  $.011$ , respectively) in DCD donors. The characteristics of recipients were similar in both groups.

### Clinical Outcomes of ECD and SCD

Five (5.2%) of 97 cases had immediate graft function; 87 recipients (89.7%) developed DGF. A significant difference was found between the ECD group and the SCD group regarding the duration of dialysis after KT (*P* = .046). BPAP-free ratios of ECD kidneys versus SCD kidneys for 1, 6, and 12 months after transplantation were 93.9% vs 97.9%, 87.4% vs 93.5%, and 87.4% vs 86.9%, respectively (Table 1), and no significant difference was found (*P* = .944). However, lowest Cr levels of the ECD group were significantly higher than those of the SCD group (*P*  $<.001$ ).

### Death-Censored Graft and Patient Survival Rates in SCD and ECD Transplants

Death-censored graft survival of ECD kidneys versus SCD kidneys for 1, 5, and 10 years after transplantation were

**Table 1. Comparison of Baseline Characteristics and Outcomes After Transplantation**

	ECD	SCD	<i>P</i> Value
N	50	47	
<b>Donor</b>			
Age (years)	60.4 $\pm$ 8.2	38.8 $\pm$ 15.0	$<.001$
Male/Female	31/19	26/21	.446*
Terminal Cr $>1.5$ mg/dL (yes/no)	34/16	22/25	.011*
Cerebrovascular events (yes/no)	37/13	17/30	$<.001$ *
Hypertension <sup>†</sup> (yes/no)	23/25	3/44	$<.001$ *
Cannulation (yes/no)	37/13	38/9	.421*
Machine perfusion (yes/no)	0/50	0/47	NA
Respirator off <sup>‡</sup> (yes/no)	6/23	7/24	.859*
Use of heparin sodium (yes/no)	50/0	47/0	NA
Use of maintaining graft-viability drugs (yes/no)	0/50	0/47	NA
<b>Recipient</b>			
Age (years)	48.4 $\pm$ 8.9	51.2 $\pm$ 7.96	.125
Male/Female	32/18	27/20	.491*
Pre-transplant dialysis interval (years)	16.6 $\pm$ 6.7	18.6 $\pm$ 6.2	.097
Times of transplantation (1st/2nd)	43/7	41/6	.858*
HLA-AB mismatch	1.7 $\pm$ 0.9	1.5 $\pm$ 1.0	.417
HLA-DR mismatch	0.2 $\pm$ 0.5	0.3 $\pm$ 0.5	.905
WIT (min)	7.7 $\pm$ 10.9	6.7 $\pm$ 9.6	.180
TIT (h)	8.6 $\pm$ 4.4	9.3 $\pm$ 4.6	.715
IGF (%)	1 (2.0)	4 (8.5)	.147*
DGF (%)	47 (94.0)	42 (89.4)	.593*
PNF (%)	2 (4.0)	1 (2.1)	.594*
Post-transplant dialysis interval (days)	12.2 $\pm$ 8.06	10.2 $\pm$ 10.4	.046
Lowest Cr level <sup>§</sup> (mg/dL)	1.8 $\pm$ 1.1	1.2 $\pm$ 1.3	$<.001$
<b>BPAP free ratio<sup>¶</sup> (%)</b>			
1-month	93.9	97.9	
6-month	87.4	93.5	
1-year	87.4	86.9	
5-year	87.4	86.9	.944
<b>Graft survival<sup>¶</sup> (%)</b>			
1-year	84.0	97.9	
5-year	74.8	95.6	
10-year	70.2	81.8	.102
<b>Patient survival<sup>¶</sup> (%)</b>			
1-year	100.0	100.0	
5-year	92.9	93.5	
10-year	79.7	90.4	.501

Mean  $\pm$  SD.

Abbreviations: Cr, creatinine; WIT, warm ischemia time; TIT, total ischemic time; NA, not applicable; IGF, immediate graft function; DGF, delayed graft function; PNF, primary non-function; BPAP, biopsy-proven acute rejection.

\*Chi-square test.

<sup>†</sup>2 patients were omitted due to an incomplete data for HTN.

<sup>‡</sup>Data on "respirator-off" were not reported in 37 cardiac death donors offered after June 2008 in a formal document disclosed by Japan Organ Transplant Network.

<sup>§</sup>Lowest level of creatinine throughout the whole observation period.

<sup>¶</sup>Log-rank test.

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