



Primary Nonfunction on Kidney Transplant Recipients From Donation After Circulatory Death Donors

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ABSTRACT

Background. The need for donor pool expansion remains an important task for kidney transplantation. The aim of this study is the evaluation of primary nonfunction (PNF) from donation after circulatory death (DCD) kidneys.

Methods. Between 1996 and 2017, 100 kidney transplants from DCD donors were conducted in our department. We retrospectively analyzed PNF of kidney transplant recipients from DCD donors in terms of donors' and recipients' epidemiologic characteristics.

Results. Of 100 grafts, 95 recipients (95.0%) had discontinued hemodialysis at the time of hospital discharge. Only 5 recipients (5.0%) developed PNF. All 5 PNF recipients received a single graft from an expanded criteria donor (ECD). The mean donor age in the PNF group was 65.0 (SD, 6.2) years. Significant differences between the PNF group and discontinued dialysis group were found for donor age ($P < .01$) and for the use of ECD kidneys ($P < .02$). Nevertheless, no significant difference was found between groups for several factors: a history of hypertension and cerebrovascular events, terminal creatinine levels, and graft weight.

Conclusion. The incidence of PNF from DCD kidneys was very low. Although ECD kidneys in older donors might be a significant risk factor for PNF, these findings suggest that DCD kidneys should be used more frequently for donor expansion.

IN the field of kidney transplantation, current statistics of end-stage renal disease patients in Japan indicate that although approximately 320,000 patients are under maintenance dialysis, kidney transplant (KTx) is performed on only 1600 patients each year. In Japan, living KTx has been the most popular modality of organ procurement. Donation after brain death donors have been increasing since the organ transplant law was revised in 2010, but that expansion is not nearly sufficient to accommodate the current organ shortage. Recent efforts are underway worldwide to expand the donor pool, including use of kidneys from expanded-criteria deceased donors after circulatory death [1,2].

Some reports have described that donation after circulatory death (DCD) kidneys present a higher percentage of primary nonfunction (PNF) and delayed graft function because of the longer agonal phase and warm ischemia time [3–5]. The agonal phase can have unfavorable effects on DCD kidneys.

Therefore, organ viability assessment must be conducted for marginal kidneys from DCD donors. This study retrospectively analyzes PNF of KTx recipients from DCD donors in terms of donor and recipient epidemiologic characteristics.

PATIENTS AND METHODS

Populations

Between 1996 and 2017, we performed 100 KTxs from DCD donors at our center at Tokyo Women's Medical University Hospital. All

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donors were Maastricht category grade III or IV. Procurement methods for grafts from DCD donors were reported previously [1,6]. Donation after withdrawal of cardiopulmonary support and medical treatment in DCD donors was unconventional until the organ transplant law was enforced in 2010. All kidneys are fundamentally accepted for KTx in our center, except for absolute contraindications. This study was conducted in accordance with the principles of the Declaration of Helsinki.

Immunosuppressive Regimens

All recipients were treated with cyclosporine-based (6 mg/kg per day) or tacrolimus-based (0.1 mg/kg per day) immunosuppression. Since 1999, mycophenolate mofetil (2000 mg/day) has been used in place of azathioprine and mizoribine. Induction therapy with basiliximab (20 mg/day on the day of surgery and on postoperative day 4) started in 2002. Methylprednisolone was administered intravenously at 250 mg on the day of surgery; then it was tapered until discontinuation, if possible, on postoperative day 14.

Definition of Expanded Criteria Donors

For this study, expanded criteria donors (ECDs) were defined as either donors older than 60 years or aged 50 to 59 years with any 2 of the following criteria: history of hypertension, cause of death from cerebrovascular events, or terminal creatinine (t-Cr) level ≥ 1.5 mg/dL.

Definition of PNF

Primary nonfunction was defined as failed function of the transplanted kidney that necessitated continued maintenance dialysis.

Statistical Analyses

Values were expressed as mean (SD). Differences were evaluated using the χ^2 test for discrete variables and the Kruskal-Wallis test or Mann-Whitney test for continuous variables. A *P* value $< .05$ was inferred as statistically significant.

RESULTS

Clinical Outcomes

Of 100 grafts from DCD donors with Maastricht categories III or IV, death-censored graft survival rates were 91% at 1 year, 87% at 5 years, and 78% at 10 years after transplant; 95 recipients (95.0%) had discontinued hemodialysis at the time of hospital discharge (Table 1). Only 5 recipients (5.0%) experienced PNF.

Donors' Epidemiologic Characteristics

All 5 PNF kidneys were extracted from ECDs: 4 donors were older than 60 years with multiple comorbidities; 1 donor aged 50 to 59 years had a history of hypertension and t-Cr ≥ 1.5 mg/dL (Tables 1 and 2). The mean donor age in PNF kidneys was 65.0 ± 6.2 years. Significant differences between the PNF group and the discontinued dialysis group were found for donor age ($P < .01$) and use of ECD kidneys ($P < .02$). Nevertheless, no significant difference was found between groups for several factors: a history of hypertension and cerebrovascular events, t-Cr levels, the prevalence of withdrawn cardiopulmonary support and prearrest cannulation, and graft weight.

Recipients' Epidemiologic Characteristics

Kidneys were allocated according to the rules of the Japan Organ Transplant Network irrespective of donor criteria. For recipients, no significant difference was found for age, sex, dialysis interval, HLA mismatch, warm ischemia time, or total ischemia time (Table 1).

DISCUSSION

The preferred treatment of choice for patients with end-stage renal disease is KTx, not dialysis. Because of the benefit of higher patient survival rate associated with KTx as opposed to survival rates for dialysis, KTx represents an

Table 1. Epidemiologic Characteristics of Donors and Recipients in Respective Groups

	Discontinued Dialysis		<i>P</i> Value
	PNF 5	95	
Donor			
Age (years)	65.0 \pm 6.2	49.5 \pm 16.0	.01
Male/female	3/2	57/38	1.00
Terminal Cr (mg/dL)	2.4 \pm 2.7	2.9 \pm 3.2	.46
Cerebrovascular events (yes/no)	4/1	52/43	.26
Hypertension* (yes/no)	4/1	26/67	.27
Expanded criteria donors (yes/no)	5/0	49/46	.02
Admission interval (days)	11.4 \pm 5.3	9.7 \pm 7.4	.32
Cannulation (yes/no)	4/1	72/23	.82
Machine perfusion (yes/no)	0/5	0/95	1.00
Respirator off ^f (yes/no)	0/3	12/45	.37
Use of heparin sodium (yes/no)	5/0	95/0	1.00
Use of maintaining graft-viability drugs (yes/no)	0/5	0/95	1.00
Primary diseases			
Cerebrovascular diseases	4	52	
Anoxic encephalopathy	1	20	.25
Cranio-cerebral trauma	0	20	
Graft weight (g)	186.2 \pm 37.7	212.6 \pm 52.2	.33
Recipient			
Age (years)	41.4 \pm 11.6	50.2 \pm 8.0	.10
Male/female	4/1	57/38	.37
Pre-transplant dialysis interval (years)	18.9 \pm 9.6	17.6 \pm 6.3	.96
Times of transplantation (1st/2nd)	5/0	82/13	.37
HLA-AB mismatch (0/1/2/3/4)	0/2/1/2/0	12/28/35/17/3	.63
HLA-DR mismatch (0/1/2)	3/2/0	73/20/2	.58
WIT (min)	10.0 \pm 13.8	8.6 \pm 10.2	.84
TIT (h)	6.2 \pm 1.8	9.1 \pm 4.5	.13

Data are presented as mean \pm SD or as otherwise indicated. Abbreviations: Cr, creatinine; PNF, primary nonfunction; SD, standard deviation; TIT, total ischemia time; WIT, warm ischemia time.

*Two patients were omitted due to incomplete data for hypertension.
^fData were not reported for 40 circulatory death donors after June 2008 in a formal document disclosed by the Japan Organ Transplant Network.

Table 2. Epidemiologic Characteristics of Primary Nonfunction Kidneys

Kidney	1	2	3	4	5
Age	74	62	52	66	66
Sex	Male	Male	Male	Female	Female
Cause of death	Cerebrovascular disease	Cerebrovascular disease	Anoxic encephalopathy	Cerebrovascular disease	Cerebrovascular disease
Terminal Cr (mg/dL)	0.9	4.8	6	0.29	0.29
Cerebrovascular events	+	+	-	+	+
Hypertension	+	-	+	+	+
Expanded criteria donors	+	+	+	+	+
Cannulation	+	+	-	+	+
Machine perfusion	-	-	-	-	-
Heparin	+	+	+	+	+
Admission Interval (day)	7	6	10	17	17
Withdrawal of life support	-	-	-	-	-
Graft weight (g)	205	230	185	160	150
Diabetes	-	-	-	-	-
Drug use					
NSAIDs	-	-	+	-	-
VCM	-	-	-	-	-
Amnoglycosides	-	-	-	-	-
Other antibiotics	CEZ	SBTPC + CLDM	MEPM + CLDM	DRPM	DRPM
Sepsis	-	-	-	-	-

Abbreviations: CEZ, cefazolin sodium; CLDM, clindamycin; Cr, creatinine; DRPM, doripenem hydrate; MEPM, meropenem hydrate; NSAID, nonsteroidal anti-inflammatory drug; SBTPC, sulfamethoxazole trimethoprim; VCM, vancomycin.

option even for patients with many risk factors [7,8]. However, the average waiting time for dialysis patients to receive kidney grafts in Japan is 13 years, as opposed to 5 years in North American and European countries [9,10]. In Japan, DCD donors are an increasingly used organ resource to alleviate chronic kidney graft shortages. Therefore, organ viability assessment is fundamentally necessary for marginal kidneys from DCD donors.

We have reported excellent long-term graft outcomes from using DCD kidneys [1,6,11,12]. From this study of our research team, we found great outcomes in terms of the PNF rate. The incidence of PNF was 5%, which was much lower than described in other studies using mainly uncontrolled DCD donors in European countries [4,13,14]. Generally, for marginal kidneys, donor age older than 60 years had negative effects not only for graft survival but also for the PNF rate in DCD [2,13,15]. We reported earlier that donor age is an independent risk factor for long-term outcomes of kidney grafts from DCD donors [1]. Additionally, in this study, 4 of 5 PNF kidneys (80%) were extracted from donors older than 60 years with comorbidities, including hypertension, cerebrovascular events, or t-Cr level ≥ 1.5 mg/dL. Results suggest that older donors represent an important risk factor affecting graft survival in DCD transplants because of the high rate of PNF incidence.

In conclusion, results show that the incidence of PNF from DCD kidneys was very low. Although ECD kidneys in older donors might constitute a significant risk factor for PNF, these findings suggest that DCD kidneys should be used more frequently for donor pool expansion.

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