Posttransplant Outcomes of Kidneys Donated After Brain Death Followed by Circulatory Death: A Cohort Study of 128 Chinese Patients

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Background. Donation after brain death followed by circulatory death (DBCD) is a new class in the unique Chinese donor classification system. Currently, in China, the organ transplantation of DBCD is rising. However, there is a dearth of research on the characteristics and outcomes of DBCD kidney transplantation. Method. We collected 128 DBCD renal transplant patients who underwent surgery between June 2013 and May 2016 at our center to analyze clinical outcomes and to share our experience to enhance perioperative management in DBCD kidney transplantation. Results. At the end of follow-up, no patients experienced primary nonfunction, but delayed graft function occurred in 25.8%. One- and 3-year graft survivals were 97.7% and 94.5%, respectively. The average length of stay was 20.88 ± 14.6 days, the incidence of posttransplant complications was 46.1% (59 patients), and 31 patients suffered more than 1 complication. In addition, the average length of stay of patients without complications and with at least 1 complication was 13.07 ± 2.01 days and 30.02 ± 17.4 days, respectively. There was a significantly higher incidence of complications associated with the postoperative hospital stay in DBCD patients. Conclusions. Patients who received a DBCD kidney demonstrated a good outcome in terms of both graft survival and graft function. Hence, DBCD is suitable for national reality and conditions and offers a feasible option for deceased-donor kidney transplantation in China. To prevent complications and reduce the duration of hospital stay, we should strengthen preoperative and postoperative management.

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Patients with end-stage renal disease (ESRD) are faced with either dialysis or organ transplantation. Maintenance dialysis involves numerous sessions; therefore, patients are advised to undergo kidney transplantation for its long-term benefits which include longer life and better quality of life.1-5 In light of the benefits of kidney transplantation, there is an urgent need to boost the supply of donor kidneys and shorten the waiting period for transplantation.6

Currently, donation after cardiac death (DCD) is considered a viable way to expand the donor pool.7-9 However, the incidence of delayed graft function (DGF) and primary nonfunction (PNF) is higher in recipients of DCD kidneys than in recipients of donation after brain death (DBD) transplantation.10,11 Because transplant surgeons have gained more experience with DCD kidney transplantation over the last decade, several reports have demonstrated equivalent

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efficacy of kidney function and graft survival between recipients of DCD and DBD kidneys.\textsuperscript{12-16}

In 2007, China implemented regulation of human organ transplantation with the aim of establishing a voluntary organ donation system and gradually abolishing the use of organs from prisoners sentenced to death. The regulation also defines cardiac death in China and establishes a legal and procedural framework for an organ donation system, based on voluntary donation after cardiac death, which adheres to Chinese social and cultural principles and complies with international transplantation standards.\textsuperscript{17} In this system, the donors can be divided into the following: China category I—DBD, China category II—DCD, and China category III—donation after brain death followed by circulatory death (DBCD). The donation of China category III provides the third option for Chinese people who wish to donate organs after death in addition to the other 2 international approaches of DBD and DCD.\textsuperscript{18} Since this regulation was introduced, the donation cases and donated organs in China have increased. However, there is a dearth of research on the characteristics and outcomes of DBCD kidney transplantation at present.

In this study, we review 128 patients who underwent DBCD kidney transplantation at our center. Our large, single-center Chinese cohort study aims to analyze the clinical outcomes after surgery and to share our initial experiences to improve perioperative management in DBCD kidney transplantation. We establish the feasibility of DBCD donation in China and show that China is moving in the right direction in terms of organ donation for patients with ESRD.

**MATERIALS AND METHODS**

**Study Population**

This retrospective study was approved by the institutional review board and ethics committee of the Third Affiliated Hospital of Sun Yat-sen University, and all research were conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all patients. Between June 2013 and May 2016, a total of 128 patients underwent DBCD kidney transplantation at our center. Patients who underwent simultaneous liver kidney transplantation or dual-kidney transplantation during this period were excluded from the study. The median follow-up time was 19 months (range, 3-36 months).

In the study, DBCD donors were according with China category III standard. In this protocol, brain death donors are processed with planned withdrawal of mechanical support and subsequent execution of cardiac death protocols. The criteria for DBCD donors were: age, younger than 40 years; warm ischemia time, less than 25 minutes; agonal time from withdrawal of mechanical ventilation or organ perfusion support to cardiac arrest, 2 hours; and no history of systemic sepsis, diabetes mellitus, malignancy, or renal disease.

All patients of kidney donation were conducted according to the protocols of China categories III donors.\textsuperscript{19} When a potential donor was identified, the care team would notify the organ procurement organization (OPO). After gaining approval for the potential donor’s family, treating physicians made the decision for discontinuation futile therapies; these processes were entirely distinct and separate from those of the transplantation surgeons and OPO members. And then, the Red Cross organ donation coordinators would discuss the details of DBCD organ donation with the patient’s immediate family, and the donation would proceed only if the donor’s immediate family members had no objections to donation. After that, neurology or intensive care unit specialists would withdraw life-sustaining supports and declare the circulatory death in the potential donor. Once asystole had been confirmed by electrocardiography for 5 minutes of “no-touch time,” donor was transferred to the surgical suite, and expeditious laparotomy was performed by surgeons from the local OPO. Rapid cannulation of the abdominal aorta allowed flushing with 3000 mL cold UW solution with 25 000 units of heparin. The kidneys were recovered and preserved by static cold storage or a machine perfusion pump (LifePort). Subsequently, the Chinese Network for Organ Sharing allocated the recovered kidneys using a policy similar to that of the United Network for Organ Sharing.

HLA typing and a complement-dependent cytotoxicity assay were routinely done before DCD kidney transplantation to prevent antibody-mediated hyperacute or accelerated rejection. Transplantation was not performed if the complement-dependent cytotoxicity result was positive.

The quality of donor kidneys was subjectively evaluated by the anatomical appearance, preflush and postflush appearance, and the clearance of blood in the venous effluent when flushing with preservative solution. Starting in 2013, some donor kidneys were evaluated using a machine perfusion pump. Kidney biopsies, followed by rapid paraffin sections, were done before transplantation if poor quality of the kidney was suspected by an abnormal postflush appearance, a high-perfusion pressure, a donor older than 40 years, or a donor with a history of hypertension or abnormal serum creatinine. The donor kidneys were discarded if machine perfusion pumping had a flow rate less than 90 mL/min or a resistance index greater than 0.4, or if the pretransplant biopsy showed greater than 20% glomerulosclerosis or interstitial fibrosis/arteriosclerosis.

Donor and recipient characteristics were collected. Postoperative complications, graft loss, and patient deaths were recorded during the follow-up period. Warm ischemia time was defined as the time from circulatory arrest to flushing with a cold preservation solution. Graft function in the early period after kidney transplantation was divided into immediate graft function, defined as the lack of a dialysis requirement after transplantation; DGF, defined as a temporary dialysis requirement in the first week after transplantation; and PNF, defined as the necessity for continuous dialysis after transplantation. The glomerular filtration rate was estimated using the abbreviated modification of diet in renal disease equation. Graft loss was defined as a permanent return to dialysis or a need for retransplantation. Renal allograft dysfunction was defined as a creatinine level greater than 150 μmol/L 2 weeks after transplantation.

**Immunosuppressive Regimen and Prophylactic Treatment**

Patients were given induction therapy as intravenous rabbit antithymocyte globulin, 50 mg/d, during surgery and on postoperative days 1 and 2. Alternatively, we used intravenous basiliximab, 20 mg/d, during surgery and on postoperative day 4 with methylprednisolone, 500 mg/d, during
surgery and on postoperative days 1 and 2, then 250 mg/d on postoperative days 3 and 4. Patients received oral myco-
phenolate mofetil, 1000 mg twice daily, after kidney trans-
plantation. Either tacrolimus or Cyclosporine A was started
on postoperative day 3. The initial tacrolimus dose was
0.1 mg/kg per day, with a trough level 5 to 10 ng/mL for
the first 6 months, then tapered to 4 to 6 ng/mL until 1 year
and 3 to 5 ng/mL after 1 year. Cyclosporine A was initiated
with a dose of 5 mg/kg per day and a trough level of 150
to 200 ng/mL for the first 6 months, then tapered to 125
PO day 1 to day 10, then oral ganciclovir, 3 g/d, was used as
prophylaxis. (5 mg/kg), for cytomegalovirus prophylaxis from postopera-
tive day 1 to day 10, then oral ganciclovir, 3 g/d, was used as
maintenance therapy until 90 days. Oral sulfamethoxazole,
500 mg/d, for three consecutive days. For steroid-resistant
rejection was treated with intravenous methylprednisolone,
200 ng/mL for the first 6 months, then tapered to 125
observed. A total of 7 recipients (5.5%) lost their renal grafts. Two
patients suffered renal-allograft rupture, and 5 had acute rejec-
tion and bleeding. Kaplan–Meier analysis showed that
the 1-year graft survival was 97.7%, and the 3-year graft sur-
vival was 94.5%. Two patients died of pneumonia after kid-
ney transplantation; patient survival was 98.4% over the
follow-up period.

**DISCUSSION**

Kidney transplantation is undoubtedly the best renal re-
placement therapy modality for most ESRD patients, al-
though the shortage of deceased donors has led to long
waiting periods. Since 2007, the Chinese government en-
deavored to establish and develop a legal framework for or-
gan donation after cardiac death, in accordance with the
World Health Organization guidelines on organ transplanta-
tion.17–20 The Health Ministry of China has made an im-
portant amendment to the donation policy by allowing DBD
and DCD organ transplantation, with excellent outcomes.21,22
However, in China, there is still a major shortage of poten-
tially suitable donor organs, due to citizens’ traditional cul-
ture, the absence of such legislation, and brain death concept
in reality society. Therefore, a uniquely Chinese donor

**RESULTS**

**Characteristics of Donors and Recipients**

A total of 128 DBCD kidneys from 69 donors were
transplanted into recipients during the study period. Ten kid-
neys were shared with other hospitals. Thirty-six DBCD kid-
neys from 18 donors (22%) were discarded due to poor
quality: microthrombosis in 26 (72.2%), severe interstitial fi-
brosis in 6 (16.7%), and severe renal-artery atherosclerosis in
4 kidneys (11.1%). The baseline characteristics of the recipi-
ents and donors are summarized in Tables 1 and 2.

**Complications After DCD Kidney Transplantation**

For all patients, the average length of stay (LOS) was
20.88 ± 14.6 days; 44 patients had a prolonged LOS (≥21
days), and 84 patients were discharged from the hospital at
less than 21 days. The longest LOS, 129 days, was in a pa-
tient diagnosed with renal allograft dysfunction and DGF.
The incidence of all complications after DBCD kidney trans-
plantation was 46.1% (59 patients): 31 patients had more
than 1 complication (18 with 2 different kinds of complica-
tions, 8 with 3 different kinds of complications, and 5 with
4 different kinds of complications), and 47 patients (79.7%)
had a prolonged LOS. A total of 24 patients (18.8%) had
renal-allograft dysfunction, 33 (25.8%) had DGF, and 5
(3.1%) had acute rejection. Other postoperative complica-
tions included pneumonia (10.9%), renal allograft rupture
(1.6%), lymphatic fistula (4.7%), peritonitis (1.6%), heart
failure (4.7%), urine leakage (0.8%), urinary infection
(1.6%), wound infection (4.7%), and psychological symp-
toms (10.2%) (Figure 1).

We also evaluated the relation between the incidence of
complications and LOS. The average LOS of patients with
at least 1 complication was 30.02 ± 17.4 days (single complica-
tion, 21.46 days; 2 complications, 31.17 days; 3 complicati-
ions, 36.12 days; 4 complications, 64 days). The average
LOS in patients without any complications was 13.07 ±
2.01 days. This comparison showed an increased incidence
of complications associated with a longer postoperative hos-
pital stay, a significantly different result (Figure 2).

**Graft and Patient Outcomes**

A total of 7 recipients (5.5%) lost their renal grafts. Two
patients suffered renal-allograft rupture, and 5 had acute rejec-
tion and bleeding. Kaplan–Meier analysis showed that
the 1-year graft survival was 97.7%, and the 3-year graft sur-
vival was 94.5%. Two patients died of pneumonia after kid-
ney transplantation; patient survival was 98.4% over the
follow-up period.

**Statistical Analysis**

Graft and patient survival was calculated using Kaplan-
Meier analysis. Statistical analysis was performed using Sta-
tistical Package for the Social Sciences (SPSS) for Windows,
version 16.0 (SPSS Inc., Chicago, IL, USA).

**TABLE 1.**

| Baseline recipient characteristics |   |
|-----------------------------------|---|
| Age, y                            | 42.20 ± 11.44 |
| Sex (male/female)                 | 90 (70.3%)/38 (29.7%) |
| BMI, kg/m²                        | 21.54 ± 3.45 |
| Dialysis status                   |   |
| Hemodialysis                      | 95 (74.2%) |
| Peritoneal dialysis               | 28 (21.9%) |
| No dialysis                       | 6 (4.7%) |
| Median dialysis time, mo          | 18.74 |
| Hemodialysis                      | 28.14 |
| Peritoneal dialysis               |   |
| Primary disease                   |   |
| Chronic glomerulonephropathy      | 103 (80.5%) |
| IgA nephropathy                   | 10 (7.8%) |
| Diabetic nephropathy              | 6 (4.7%) |
| Other                             | 9 (7%) |
| HLA mismatched (loci)             | 2.4 ± 1.3 |

Values are presented as the mean ± SD or as number (percentage).

BMI, body mass index; IgA, immunoglobulin A.
A classification system has been established, which is suitable for national reality and conditions. The obvious difference between the Chinese donor classification and international common practice is China category III—DBCD. Although China category III—DBCD can be categorized as DCD, it is distinct from both the conventional DBD (does not involve planned cardiac arrest) and Maastricht category IV (does not involve planned, predictable cardiac arrest after brain death). In this category, the donors satisfied the DBD criteria, but whose family members do not agree to donation with the heart still beating or the physicians cannot declare the brain death due to various reasons, and then the potential donors withdraw the futile therapies and life-sustaining supports and wait for the declaration of death using circulatory death criteria. In addition, DBCD protocol also enables abdominal organ recovery after the implementation of extracorporeal membrane oxygenation to reduce ischemic injuries to transplantable organs. The use of extracorporeal membrane oxygenation is ethically permitted before asystole because the patient’s clinical condition fulfills the criteria of brain death. All of these processes are controlled. However, Modified Maastricht classification III (anticipated cardiac arrest) does not need to fulfill the criteria of brain death and does not initiate extracorporeal membrane oxygenation after the patient is declared dead by permanent absence of circulation. The DBCD category is possible for extensive discussion with the potential donors’ family and prospective allocation of organs, removal of life support timed with arrival of the procurement team, and minimizing warm and cold ischemia time. In addition, in China, DBCD is likely to influence the citizens to gradually accept the concept and practice of brain death.

With these reports, we investigated recent studies and collected the relevant results on DBCD kidney transplantation in China. According to Summers et al’s research, graft survival rates up to 5 years are 85.1% in DCD kidneys and 83.2% in DBD kidneys. The difference between Summers’ results and ours is that most of our donors were China category III—DBCD (which is similar but different from Maastricht category IV, also categorized as DCD). In addition, increasing donor age is regarded as an independent risk factor for poor graft outcome in recipients of kidneys from both DCD and DBD donors, and our donors were slightly younger than those in Summer et al’s study. Finally, increasing cold ischemic time is a potential risk factor for graft survival in DCD.

### TABLE 2: Baseline donor characteristics

| Characteristic                          | Value                  |
|----------------------------------------|------------------------|
| Age, y                                 | 31.72 ± 15.23          |
| Sex (male/female)                      | 40 (58%)/29 (42%)      |
| BMI, kg/m²                             | 23.36 ± 4.16           |
| Primary disease                        |                        |
| Craniocerebral trauma                  | 32 (46.4%)             |
| Cerebrovascular disease                | 28 (40.6%)             |
| Anoxic encephalopathy                  | 9 (13%)                |
| History of hypertension                | 8 (11.6%)              |
| Serum creatinine level before recovery, μmol/L | 166.33 ± 138.42  |
| Warm ischemia time, min                | 13.4 ± 1.7             |
| Cold ischemia time, h                  | 11.5 ± 2.7             |
| Use of vasoactive drugs                | 29 (42%)               |

Values are presented as the mean ± SD or as number (percentage).

![FIGURE 1](image1.png)  
**FIGURE 1.** Patients with complications and LOS after kidney transplantation.

![FIGURE 2](image2.png)  
**FIGURE 2.** Mean LOS in patients with complications; the incidence of complications increased significantly with increasing length of postoperative hospital stay (*P* < 0.05).
kidney transplantation, and our cold ischemic times were shorter than those in Summer et al's study. Therefore, we might be expected to have different outcomes.

None of our patients experienced PNF, and only 25.8% suffered DGF after DBCD kidney transplantation. In European countries, the incidence of DGF is about 30% to 84%, quite a bit higher than that seen at our center. In fact, the DGF rate in China is significantly lower than that seen in Western countries. All DBCD donors at our center were labeled and under controlled; however, some patients in Western countries are uncontrolled. Meanwhile, our center has slightly shorter warm and cold ischemia times than those seen in Western countries. Our average warm ischemia time was 13.4 minutes versus 25 minutes in European reports, and our average cold ischemia time was 11.5 hours versus 16.8 hours in European studies. The reasons for our shorter times include the fact that, to ensure adequate transplant center infrastructure, our center has a surgical intensive care unit (SICU) and surgical suite dedicated to transplantation. Once the organ is collected within the “no touch time” or further delay in organ disposition, our donors are collected from the SICU and transferred immediately to the surgical suite. This limits the warm ischemia time to less than 20 minutes. In addition, we endeavor to reduce the time taken for crossmatch testing before transplantation to reduce cold ischemia time. Unlike in Western countries, most of our DBCD kidneys are collected from local hospitals, this shortens the organ transport time compared with broader organ sharing policies. Our much younger patient age is another factor. Finally, we used pretransplant graft biopsies to ensure the quality of renal allografts, discarding poor-quality grafts and those with a warm ischemia time longer than 25 minutes. It is fair to say that our DFG and PNF rates after DBCD kidney transplantation are lower than those seen in European countries.

Our research also focused on complications after transplantation; the 59 patients who suffered complications after surgery might have longer postoperative hospital stays. A longer LOS is a known risk factor for infection in patients who are prone to hospital-acquired infections; increased LOS also confers a higher probability of having any kind of complication, possibly inciting a vicious cycle and having a harmful impact on patient recuperation. Recipients who are in critical condition have lower immunity because of numerous and long periods of dialysis and high doses of corticosteroid therapy and other induction treatments; therefore, these patients are most likely to suffer a series of harmful complications after transplantation, especially given the use of antirejection treatment. To prevent this vicious cycle and strengthen preoperative and postoperative management, we recommend detailed preoperative surgical preparation, meticulous surgical technique, systemizing an intensive monitoring program, and developing personalized therapy during the recovery period. Following these recommendations should minimize the occurrence and progression of complications. Otherwise, due to the difference in concept of rehabilitation, patients in China are expected of the creatinine recovered into the normal range and calcineurin inhibitor adjusted in stable doses during the hospitalization, the average LOS after transplantation in our study was much longer in comparison of western studies. Nevertheless, at this stage, we have only begun to investigate; further research is required into patient prognosis and long-term complications after DCD kidney transplantation.

In conclusion, patients who receive kidneys from DBCD under specific parameters have good outcomes in terms of both graft survival and graft function. DBCD donation offers a feasible option for deceased-donor transplantation, and more widespread implementation of DBCD may further increase the life expectancy of patients with ESRD by reducing the waiting period for transplantation. Meanwhile, to prevent complications and reduce the duration of hospital stay, we should enhance preoperative and postoperative management.

With a transplantation process that is transparent to the general public and improved over the previous system, we are delighted to see that China is moving in the right direction. Although opportunities and challenges coexist, with the joint effort of the Chinese government, the Ministry of Health, the Red Cross, the Chinese Transplantation Society, and the international community, we have faith that DBCD kidney transplantation has a bright future in China.

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