CLINICAL RESEARCH

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Accepte	ed: 2017.01.09 ed: 2017.01.09 ed: 2017.08.03		Confirmed Transmission Infection to Kidney Tran Donated After Cardiac I China: A Single-Center	nsplant Recipients from Death (DCD) Donors in				
[Stat Data Manuscr Lit	ors' Contribution: Study Design A Data Collection B Istical Analysis C Interpretation D ipt Preparation E cerature Search F unds Collection G	BF 1 ADF 2	Huanmiao Liu Shaojun Ye	 Department of Transplant Surgery, The Third Xiangya Hospital, Central South University, Changsha, Hunan, P.R. China Zhongnan Hospital of Wuhan University, Institute of Hepatobiliary Diseases of Wuhan University, Transplant Center of Wuhan University, Hubei Key Laboratory of Medical Technology on Transplantation, Wuhan, Hubei, P.R. China 				
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Background: Material/Methods:		-	We aimed to investigate blood and urine cultures of donated after cardiac death (DCD) donors and report the cases of confirmed (proven/probable) transmission of bacterial or fungal infection from donors to kidney recipients. Seventy-eight DCD donors between 2010 and 2016 were included. Sixty-one DCD donors underwent blood cultures and 22 episodes of bacteremias developed in 18 donors. Forty-three donors underwent urine cultures					
	I	Results:	Inappropriate use of antibiotics in donor was a risk FK506 was more frequent in recipients without donor (p =0.033). Recipients with donor-derived infection we and 28.6%, respectively), when compared with those ney recipients with donor-derived infection died; one	confirmed donor-derived bacterial or fungal infections. factor for donor-derived infection (p =0.048). The use of -derived infection than those with donor-derived infection ere associated with higher mortality and graft loss (42.9% e without donor-derived infection (4.8% each). Three kid- e death was due to multi-organ failure caused by <i>Candida</i> al artery; two of them did not receive appropriate antimi-				
	Conc	'Contribution: ACE 1 Qiquan trudy Design A BF 1 Huanmi ta Collection B ADF 2 Shaojur ical Analysis C br 1 Huanmi terpretation D Preparation E ADF 2 Shaojur Ye, Preparation E Source of support: Shaojun Ye, Background: We aimed the cases Katerial/Methods: Seventy-ei Conclusions: Our kidney Material/Methods: Seven of Inappropri FK506 was (p=0.033). and 28.6% ney recipie albicans, a crobial the Our kidney infection v majority o after infection v majority o And SH Keywords: Bacterial Full-text PDF: https://www.advection	infection were associated with higher mortality and g	of donor-derived infection. Recipients with donor-derived graft loss than those without donor-derived infection. The ho died did not receive appropriate antimicrobial therapy				
	MeSH Key	words:	Bacterial Infections • Disease Transmission, Infec Unrelated Donors	tious • Kidney Transplantation • Mycoses •				
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Confirmed Transmission of Bacterial or Fungal



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Background

Kidney transplantation is currently considered the definitive treatment for patients with end-stage kidney disease with well-documented survival benefits over dialysis [1]. With a limited donor pool and an expanding transplant waiting list, consideration of organs from infected donated after donor cardiac death (DCD) is necessary [2–5]. However, the utilization of organs from donors not meeting standard donor criteria has been associated with infections transmitted by the transplanted organs [6,7]. The overall safety and favorable outcomes related to donor-transmitted bacterial infections among solid organ transplantation have been reported [8,9].

Although the transmission of infections from a donor to a recipient is a rare complication of kidney transplantation, it is typically associated with significant mortality (more than 17%) [10–16].

Currently, the data on DCD donor-derived bacterial or fungal infections are lacking in China. We aimed to investigate blood and urine cultures of DCD donors and report the cases of confirmed (proven/probable) transmission of bacterial or fungal infection from donors to kidney recipients. Our present study represents the largest sample size of kidney recipients experiencing confirmed donor-derived fungal or bacterial infections reported by a single transplant center thus far.

Material and Methods

Study population

A retrospective study, at a single center, was conducted with the purpose of recording all cases of donor-derived bacterial and fungal infections between January 1, 2010 and April 1, 2016. We did not monitor cytomegalovirus and Epstein-Barr virus in every donor, however, we monitored hepatitis B virus (HBV) and hepatitis C virus in every donor and recipient, and found 15 donors underwent HBV infection and no donors developed hepatitis C virus infection when the grafts were procured. Three kidney recipients who had HBV infection before transplantation underwent relapse of HBV infection under the treatment of anti-HBV treatment. All these three recipients obtained kidney grafts from donors with HBV infection. We could not confirm these three recipients with donor-derived HBV infection. Thus, we did not include donor-derived viral infection in this cohort.

The study population consisted of 154 kidney recipients of grafts from 78 DCD donors, who were admitted into intensive care unit (ICU) of the Department of Transplant Surgery, the Third Xiangya Hospital of Central South University, Changsha, China, before organ procurement and transplantation. Multiorgan transplant recipients were excluded from the study. Data collections included donor age, gender, length of ICU stay, number of donors with/without available results of blood or urinary cultures, bacteria and fungi isolated from donors, site of infection, antibiotic administration, and cause of death. Variables associated with the recipients with donor-derived infection were collected from their medical records: age, gender, underlying kidney diseases, site of infection, time of infection onset, organisms, antimicrobial use, immunosuppressive therapy, evaluated glomerular filtration rate (eGFR) at one week after transplantation, serum creatinine level before hospital discharge or death, and crude mortality/graft loss. Maintenance immunosuppression was tacrolimus/cyclosporin-based and was complemented with mycophenolate mofetil and prednisone tapered to 5-10 mg/day. The clinical course of recipients was followed for at least six months after the onset of infection. The Ethics Committee of the Third Xiangya Hospital approved this study (tHIRB number: 2016-S249).

Definition

Transmission of the organisms was confirmed (proven/probable) when bacterial or fungal isolates from donor and at least one of the kidney recipient or two recipients from the same donor showed a similar resistance profile and when the absence of pre-transplant infectious disease in the recipients was documented [17]. Appropriate antimicrobial use in donors was considered when the infected donor receives targeted antimicrobial treatment for at least 24-48 hours, optimally with some degree of clinical response (improved white blood cell count, improved hemodynamics, defervescence) [18]. Appropriate antimicrobial use in recipients was considered if organisms isolated were in vitro susceptible to empirical antibiotics, which were administered within 48 hours of sampling for culture [19]. Death was regarded as infection-related when it was associated with clinical signs of active infection without evidence of any other cause [20].

Statistical analysis

Continuous variables were expressed as mean \pm standard deviations or median (interquartile range [IQR]). Mann-Whitney U-test or *t*-test was used for continuous variables and chi-squared test or Fisher exact test was used for comparison of categorical and binary variables, as appropriate. Univariate analysis was applied to examine the association between variables from donors or recipients and donor-derived infection. Statistical analyses were performed using the statistical package SPSS version 22.0 for Windows (SPSS Inc., Chicago, IL, USA). A *p* value <0.05 was considered statistically significant, and all tests of significance were two tailed.

Table 1. The characteristic of 78 DCD donors.

Characteristics	Value
Median age (range, years)	33.5 (2–62)
Sex, number of male/number of female	61/17
Origin of death	
Н	35
CNS benign tumor	20
CVA	18
Anoxia	4
Meningitis	1
ICU stay, median days (IQR)	5 (2.8–11.0)
Donors with positive culture	
Positive blood culture	12
Positive urine culture	8
Positive blood + urine culture	6
Blood culture, number of donors with/without available results	61/78
Appropriate antimicrobial use donors/all donors with positive blood culture results	13/18
Urine culture, number of donors with/without available results	43/78
Appropriate antimicrobial use donors/all donors with positive urine culture results	9/14
No available results for both bloodstream and urine cultures	13/78

DCD – donated after cardiac death; HI – head injury; CNS – central nervous system; CVA – cerebrovascular accident; ICU – intensive care unit; IQR – interquartile range.

Results

There were 154 kidney recipients of graft from 78 DCD donors during the study period. Four out of 26 (15.4%) donors with urinary and/or bloodstream infections developed confirmed transmission of bacterial or fungal infections, affecting seven kidney recipients and resulting in three crude mortality including at least one infection-related death.

Donor characteristics and the risk factors of donor for donor-derived infection

The characteristics of the donors are shown in Table 1. The median age was 33.5 years with a gender distribution of 61 males/17 females (sex ratio 3.6). The most common origin of death was head injury, followed by central nervous system benign tumor. Thirteen of 78 donors did not available results for both bloodstream and urine cultures. Screening results for blood and urine cultures were available for 61 (77.2%) and 43 (54.4%) DCD donors, respectively. Twenty-two episodes of bloodstream infections and 17 episodes of urinary

infections developed in 18 and 14 donors, respectively. The number of donors with a positive culture of blood and urine alone, and in combination, was 12, eight, and six, respectively. Appropriate antimicrobial use in donors with positive blood and urine culture results were 13/18 and 9/14, respectively. Results of urinary and blood cultures of the donors are shown in Table 2. The majority (63.6%; 14/22) of pathogens isolated from donor's blood were coagulase-negative *staphylococcci* and *Staphylococcus aureus*.

The comparison of the characteristics of four DCD donors resulting in infectious transmissions with 74 DCD donors without leading to transmissions is shown in Table 3. We did not find a difference in age, gender, origin of death, ICU stay, site of infection, type of organisms, resistant to antimicrobial drugs, and creatinine level before graft procured between donors with and without leading to infectious transmissions. However, the inappropriate use of antibiotics in donors was a risk factor for donor-derived infection (p=0.048). Table 2. Classification and percentage of organisms from donors.

Organisms	Strain (n=39)	Percentage
Blood culture	22	56.4
Gram-positive bacteria	15	38.5
Staphylococcus aureus	3	7.7
Enterococcus faecalis	1	2.6
Coagulase Negative Staphylococci	11	28.2
Staphylococcus epidermidis	4	10.3
Staphylococcus hemolyticus	2	5.1
Staphylococcus capitis	2	5.1
Staphylococcus cohnii	1	2.6
Staphylococcus hominis	1	2.6
Staphylococcus simulans	1	2.6
Gram-negative bacteria	4	10.3
Klebsiella pneumoniae	2	5.1
Escherichia coli	1	2.6
Acinetobacter baumannii	1	2.6
Fungi	3	7.7
Candida albicans	2	5.1
Candida parapsilosis	1	2.6
Irine culture	17	43.6
Gram-positive bacteria	4	10.3
Enterococcus faecalis	2	5.1
Staphylococcus aureus	1	2.6
Staphylococcus chromogenes	1	2.6
Gram-negative bacteria	5	12.8
Acinetobacter baumannii	2	5.1
Pseudomonas aeruginosa	2	5.1
Klebsiella pneumoniae	1	2.6
Fungi	8	20.5
Candida albicans	5	12.8
Candida parapsilosis	2	5.1
Candida krusei	1	2.6

The characteristics of recipients with donor-derived infection

Table 4 showed the characteristics of the donors and the corresponding kidney recipients to make a clearer relationship between donors and recipients. Seven kidney recipients developed confirmed donor-derived bacterial or fungal infections. Recipients 1 and 2 were classified as a proven donor-derived infection and recipients 3 through 7 were classified as a probable donor-derived infection.

Several cultures (blood, urine, and organ-space surgical site infections) were routinely taken following kidney transplantation. Transmitted pathogens included *Klebsiella pneumoniae* in three cases, and *Staphylococcus aureus* and *Candida albicans* each in two cases. No recipient had a presumed or confirmed

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Table 3. The comparison of the characteristic of 4 DCD donors resulting in infectious transmissions with 74 DCD donors without	
leading to transmissions.	

Characteristics		ulting in infectious nissions (n=4)		thout leading to ssions (n=74)	Ρ
Age, mean years ±SD	36	.25±20.27	32.	15±15.25	0.602
Male sex, n (%)	4	(100%)	57	(77%)	0.278
Origin of death, n (%)					0.237
HI	1	(25%)	34	(45.9%)	
CNS benign tumor	1	(25%)	19	(25.7%)	
CVA	1	(25%)	17	(23%)	
The others	1	(25%)	4	(5.4%)	
ICU stay, median days (IQR)	11	(7.25–16.25)	4	(2–10.25)	0.212
Site of infection ^a , n (%)					0.916
Positive urine and/or blood culture 6	1	(25%)	25	(33.8%)	
Negative culture for urine and/or blood	3	(75%)	36	(48.6%)	
Type of organisms ^b , n (%)					0.666
Bacteria+ Fungi	1	(25%)	35	(47.3%)	
Negative culture	3	(75%)	36	(48.6%)	
Resistant to multiple antimicrobics ^c , n (%)	0	(0%)	16	(21.6%)	0.576
Inappropriate use of antibiotics ^d , n (%)	2	(50%)	5	(6.8%)	0.048
Creatinine level before graft procured, median μ mol/L (IQR) 42	(23.25–57)	51	(35–77.25)	0.326

DCD – donated after cardiac death; HI – head injury; CNS – central nervous system; CVA – cerebrovascular accident; ICU – intensive care unit; IQR, interquartile range. ^{a,b,c,d} Only 65 kidney recipients who had available blood and/or urine culture were analyzed.

Table 4. The characteristics of the donors and the corresponding kidney recipients.

Donor	Diagnosis	Culture result	Inappropriate antimicrobics	Recipient	Culture result	Inappropriate antimircotics	Outcome				
		Calhicanc		R1	C. albicans (urine)	Yes	Patient/graft survival				
D1	Anoxia	C. albicans (urine + blood)	Yes	R2	C. albicans (urine + blood)	Yes	Patient died/ normal graft function				
D2	HI	Negative (urine + blood)	Negative	Negative	Negative	Negative	Yes	R3 a	K. pneumoniae (OSSS)	No	Patient died/ graft loss
DZ	пі		fes	R4 a	K. pneumoniae (OSSS)	No	Patient/graft survival				
D3	HI	Negative (urine + blood)	No	R5 b	K. pneumoniae (blood)	Yes	Patient died/ graft loss				
D 4	CNS tumor	Negative	No	R6	S. aureus (OSSS)	Yes	Patient/graft survival				
D 4		(urine + blood)		R7	S. aureus (OSSS)	No	Patient/graft survival				

HI – head injury; OSSS – organ-space surgical site; CNS – central nervous system. ^a The liver recipient of graft from the same donor as these two kidney recipients underwent bloodstream infection and peritonitis owing to *Klebsiella pneumoniae* immediately after transplantation; ^b The liver recipient of graft from the same donor as this kidney recipient also underwent bloodstream infection owing to *Klebsiella pneumoniae* immediately after transplantation.

Table 5. Characteristics, underlying kidney diseases, results of cultures and outcome of the 7 kidney recipients with DCD donorderived infections.

Characteristics		Value
Median age (range, years)	45	(20–62)
Sex, number of male/number of female		5/2
Underlying kidney diseases		
Chronic glomerulonephritis	4	(57.1)
Diabetic nephropathy	2	(28.6)
Polycystic kidney disease	1	(14.3)
Patient immunosuppressant treatment, no. of cases (%)		
ATG or ALG + FK506 + MMF + Pred	4	(57.1)
FK506 + MMF + Pred	1	(14.3)
ALG + CSA + MMF + Pred	1	(14.3)
CSA + MMF + Pred	1	(14.3)
Site of infection, no. of cases (%)		
Organ-space surgical site infections	4	(57.1)
Blood	1	(14.3)
Urinary tract	1	(14.3)
Multiple culture-positive sites ^a	1	(14.3)
Organisms		
Klebsiella pneumoniae	3	(42.9)
Candida albicans	2	(28.6)
Staphylococcus aureus	2	(28.6)
Time of infection onset, median days (interquartile range)	8	(2–10)
Serum creatinine at discharge or death, median (µmol) (interquartile range)	207	(113–621)
Appropriate antimicrobial use, no. of cases (%)	3	(42.9)
Crude hospital mortality, no. of cases (%)	3	(42.9)

DCD – donated after cardiac death; ATG – antithymocyte globulin; ALG – antilymphocyte globulin; FK506 – tacrolimus; MMF – mycophenolat mofetil; Pred – prednison; CSA – cyclosporine A. ^a One bacteremia+urinary tract infection due to *Candida albicans*.

invasive bacterial or fungal infection pre-transplantation. Two *Candida albicans* rods isolated from recipients with donor-derived infection were susceptible to the common used antifungal drugs whereas three *Klebsiella pneumoniae* specimens were multidrug resistant (MDR) and two *Staphylococcus aureus* specimens were methicillin-resistant.

Three out of seven recipients who had donor-derived infections received appropriate anti-microbial therapy. Two of three cases of *Klebsiella pneumoniae* transmission received appropriate anti-microbial therapy. One case who did not receive appropriate therapy died with graft loss. Two of four donors who

received appropriate therapy resulted in infectious transmission in three kidney recipients, one with bloodstream infection owing to MDR *Klebsiella pneumoniae* and two with organspace surgical site infections caused by methicillin-resistant *Staphylococcus aureus* (Table 4).

Underlying kidney diseases of these seven recipients consisted of three chronic glomerulonephritis cases, two diabetic nephropathy cases, and one polycystic kidney disease case. All these patients received similar postoperative intensive care with a routine triple immunosuppressive regimen including corticosteroids (n=7), mycophenolate mofetil (n=7), and FK506

Characteristics		ith donor-derived tion (n=7)	Recipients derived in	Ρ	
Age, mean years ±SD	44.86±15.18		39.41±10.93		0.205
Male sex, n (%)	5	(71.4%)	105	(71.4%)	1.000
ALG or ATG induction therapy, n (%)	5	(71.4%)	99	(67.3%)	0.308
The use of FK506, n (%)	5	(71.4%)	142	(96.6%)	0.033
eGFR level 1 week after transplantation, median ml/min/1.73 m² (interquartile range)	9.27	(5.96–50)	45.58 (18.05–71.51)	0.14
Recipient death, n (%)	3	(42.9%)	7	(4.8%)	<0.001
Graft loss, n (%)	2	(28.6%)	7	(4.8%)	<0.001

Table 6. Characteristics of 154 kidney recipients with or without donor-derived infection.

SD - standard deviation; ALG - antilymphocyte; ATG - antithymocyte; FK506 - tacrolimus; eGFR - evaluated glomerular filtration rate.

(tacrolimus) (n=6) or cyclosporine (n=1). In addition, six patients received antithymocyte or antilymphocyte globulin during the induction phase of immunosuppression after kidney transplantation. Time to onset of donor-derived infection was a median of eight days (IQR 2–10). All donor-derived infection occurred within one month post-transplantation (from 1–20 days). Organ-space surgical site infections were the predominant site of infection (57.1%). The characteristics, underlying kidney disease, and urinary and blood culture results concerning the seven patients with donor-derived infection are shown in Table 5.

Outcomes of kidney recipients with donor-derived infection

Among the kidney recipients with donor-derived infection during the at least six months of follow-up, there was a strikingly high crude mortality rate of 42.9% (3/7); one kidney recipient died due to multi-organ failure two months after combined transmission of candida urinary tract infection and candidemia and two patients died owing to rupture of the renal artery. Ultrasonography result of the patient with rupture of the renal artery was not consistent with mycotic aneurysm. The culture of the organ-space surgical site showed only an isolated growth of Klebsiella Pneumonia in one patient with renal artery rupture. Thus Klebsiella Pneumonia was the most probable causative microorganism leading to this episode of renal artery rupture. This patient died of sudden bleeding from the renal artery and we could not confirm that the renal artery rupture was secondary to Klebsiella Pneumonia. Two recipients did not receive appropriate antimicrobial therapy after infection among these three patients who died. Of three recipients with crude hospital mortality, all developed allograft dysfunction, and the serum creatinine level of two of them was more than 600 µmol/L at the point of death (serum creatinine were 207, 629, and 621 µmol/L, respectively).

The comparison of the characteristics of kidney recipients with and without donor-derived infection

Table 6 shows the characteristics of kidney recipients with donor-derived infection compared with those without donor-derived infection. The use of FK506 was less frequent in patients with donor-derived infection (71.4%) compared with those without donor-derived infection (96.6%). Recipients with donor-derived infection (96.6%). Recipients with donor-derived infection were associated with higher mortality and graft loss (42.9% and 28.6%, respectively), when compared with those without donor-derived infection (4.8% each) (p<0.001 each). Seven out of 147 kidney recipients without donor-derived infection died. Among them, six died of pneumonia or bloodstream infections caused by *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Streptococcus anginosus*, or *Staphylococcus haemolyticus*. No deaths in the rest of the cohort were secondary to infection from similar organisms isolated from recipients with donor-derived infection.

Discussion

Although there are numerous reports of fatal donor-derived infection affecting around 3% of solid organ transplants, the use of grafts from infection risk donors represents a strategy to expand the limited donor pool [21]. Since prolonged duration of dialysis is a crucial risk factor for patient mortality, it is logical to infer that increasing utilization of infection risk kidneys can shorten waiting times and improve long-term patient outcomes [22,23].

More recent data suggest that bacteremic donors may be considered, provided bacteremia in the donor was ideally treated and resolved prior to transplantation or the donor received appropriate antimicrobial treatment for at least 48 hours and antibiotic therapy was continued in the organ recipient [6,8,9,24,25]. Our present study found 29.5% (18/61) of donors (who had available results of blood cultures) developed bloodstream infections and only two kidney recipients were associated with donor-derived bloodstream infection, which is in line with literature reports suggesting that about 5% of all deceased donors have unrecognized bacteremia at the time of donation but that few instances are associated with recipient disease [8,25,26]. However, in a review of 610 liver transplants, 69 donors had bloodstream infections prior to procurement and in four (5.8%), there was transmission to the recipient despite directed antimicrobial prophylaxis [6].

Our kidney recipients had a higher occurrence rate of donorderived infection (4.5%) than the previous reports. This apparent discrepancy might be due to inadequate sample size. Furthermore, in some centers, cases that are associated with less severe disease (e.g., transient bacteremia that responds quickly to therapy) are likely to be under-recognized and, therefore under-reporting may be significant [27]. Furthermore, a thorough review of cultures for all kidney recipients of organs from DCD donors has now been implemented at our institute. The high occurrence rate of infectious transmission is not surprising since every kidney recipient in our center underwent routine surveillance cultures of urine, blood, and drainage fluid of organ-space surgical site post-transplant even if the recipients lacked symptoms of active infections. Meanwhile, our donors' infection rate was higher than other centers, which contributed to a higher occurrence rate of donor derived infectious transmission [4]. The 2013 report [28] from the Organ Procurement and Transplantation Network (OPTN) Ad Hoc Disease Transmission Advisory Committee revealed that 15 out of 117 (12.8%) donors with infections developed proven/probable transmission of bacterial (except for tuberculosis) and fungal infections, which agreed with our present occurrence rate of 4/26 (15.4%).

We found all donor-derived bacterial and fungal infections occurred within one month post-transplantation, which was accordant with a review of the Disease Transmission Advisory Committee experience from 2008–2012 which claimed the majority (86%) of transmission of bacterial and fungal infections developed within one month post-transplant [29].

Several studies reported that coagulase-negative *staphylococci* (such as *Staphylococcus epidermidis*) and *Staphylococcus aureus*, represent more commonly isolated microorganisms from donor blood cultures [9,25,26]. We also found the majority (63.6%; 14 of 22 pathogens isolated from donor blood cultures) were coagulase-negative *staphylococci* and *Staphylococcus aureus*. Our present study found two kidney recipients with donor-derived infection due to *Staphylococcus aureus*. To date, there have been several reports of suspected donor-transmitted *Staphylococcus aureus* infections in SOT recipients [7,30–32].

However, Ison et al. suggested there was a low risk of transmission of coagulase-negative *staphylococci* from a donor to a recipient [8]. Likewise, none of 11 donors with coagulasenegative *staphylococci* in our cohort developed proven/probable transmission.

We found inappropriate use of antibiotics in donor was a risk factor for donor-derived infection. We also found the use of FK506 was more frequent in recipients without donor-derived infection than those with donor-derived infection. It is not surprising that inappropriate use of antibiotics in donors was associated with more donor-derived infections. However, it is not clear why the use of FK506 was more frequent in recipients without donor-derived infection than those with donor-derived infection. We did not investigate the immunosuppression level in this study which may at least partly explain this finding.

Candida spp. transmitted from donors to the recipients was reported to be more prone to cause fatal early post-transplant complications, such as bloodstream infection or mycotic aneurysm [33]. A growing body of evidence reveals that donor-derived fungal infections are a significant complication in kidney recipients that can be related to grave even fatal outcomes with mortality rate of up to 100% [11–14,16,34]. In our present study, 1/2 (50%) kidney recipient with fungal infection died due to combined transmission of candida urinary tract infection and candidemia.

Outcomes of recipients with donor-derived infection caused by bacteria, in particular resistant bacteria, were also quite poor [10,15,35]. Lewis et al. summarized all published cases and found the mortality rate for those who developed a MDR bacterial donor-derived infection was 33% [36]. Two (40%) recipients with MDR *Klebsiella pneumoniae* infection died related to rupture of the renal artery in our present study.

Our kidney recipients with donor-derived infection showed a high morbidity (4.5%) and crude mortality (42.9%). The majority of recipients with donor-derived infection who died did not receive appropriate antimicrobial therapy after infection. Recipients with donor-derived infection were associated with higher mortality and graft loss (42.9% and 28.6%, respectively), when compared with those without donor-derived infection (4.8% each) with a follow-up time of at least six months. Our findings agreed with the data reported to the United States OPTN from 2005 to 2011 which showed the donor-derived infection-attributable recipient mortality rate of 29.2% (19/65) [8]. We need further data to assess the effect of donor-derived bacterial or fungal infections and inappropriate antimicrobial use on allograft function and recipient survival over a long-term follow up.

Currently, transplant centers in China are not required to report infectious transmission so that any data available relies on voluntary reporting by individual centers. Our present study, however, revealed that because both the morbidity and mortality of donor-derived infection are high in China, this advocates for a better understanding of potential risks for disease transmission and underpins the necessity for a standardized critical incident reporting system in the Chinese transplant system to improve short- and long-term allograft and recipient's survival.

To the best of our knowledge, our present study represents the largest sample size of kidney recipients with confirmed donor-derived fungal or bacterial infections reported by a single transplant center thus far. The principal limitation of our study was a single-center study and its retrospective nature which did not allow us to demonstrate by genetic or molecular analysis that bacteria or fungi affecting the DCD donors were the source of infection in the kidney recipients. Since we used drug-sensitive test screening for donor-derived infection rather than a gene level it is possible that our testing algorithm over-estimated the transmission events.

We need to change the policy in our institute to prevent donorderived infection. First, surveillance culture of urine and blood should be performed periodically in every donor, in particular at the time of organ procurement. Donors should be treated for 24–48 hours with antibiotics directed at the identified bacteria or fungi prior to procurement, optimally with evidence of clinical improvement. Second, the preservation fluid sample

References:

- Wolfe RA, Ashby VB, Milford EL et al: Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. N Engl J Med, 1999; 341: 1725–30
- 2. Wadei HM, Heckman MG, Rawal B et al: Comparison of kidney function between donation after cardiac death and donation after brain death kidney transplantation. Transplantation, 2013; 96: 274–81
- Schweitzer EJ, Perencevich EN, Philosophe B et al: Estimated benefits of transplantation of kidneys from donors at increased risk for HIV or hepatitis C infection. Am J Transplant, 2007: 7(6): 1515–25
- Limkemann AJ, Wolfe L, Sharma A et al: Outcomes of kidney transplants and risk of infection transmission from increased infectious risk donors. Clin Transplant, 2016; 30(8): 886–93
- 5. Wolfe RA, Roys EC, Merion RM: Trends in organ donation and transplantation in the United States, 1999–2008. Am J Transplant, 2010; 10: 961–72
- Cerutti E, Stratta C, Romagnoli R et al: Bacterial- and fungal positive cultures in organ donors: Clinical impact in liver transplantation. Liver Transpl, 2006; 12: 1253–59
- Doucette KE, Al-Saif M, Kneteman N et al: Donor-derived bacteremia in liver transplant recipients despite antibiotic prophylaxis. Am J Transplant, 2013; 13: 1080–83
- Ison MG, Grossi P: Practice ASTIDCo: Donor-derived infection in solid organ transplantation. Am J Transplant, 2013; 13: 22–30
- 9. Freeman RB, Giatras I, Falagas ME et al: Outcome of transplantation of organs procured from bacteremic donors. Transplantation, 1999; 68: 1107–11
- 10. Orlando G, Di Cocco P, Gravante G et al: Fatal hemorrhage in two renal graft recipients with multi-drug resistant *Pseudomonas aeruginosa* infection. Transpl Infect Dis, 2009; 11: 442–47

should be cultured. Finally, the recipients should be treated for 7–14 days post-transplant with antibiotics directed at the cultured bacteria isolated from donors or the preservation fluid samples. Antifungal therapy directed at the identified fungi should continue for more than two weeks unless there is no clinical or microbiologic evidence of infection.

Conclusions

DCD donors had high bacterial or fungal infection with Grampositive bacteria being predominant isolates whereas kidney recipients had a Gram-negative predominant donor-derived infection. Our findings strongly supported organ donation as the common source of bacterial or fungal infection in the kidney recipients. We found inappropriate use of antibiotics in donors was a risk factor for donor-derived infection. Furthermore, our kidney recipients with donor-derived infection showed a higher crude mortality and graft loss than those without donor-derived infection. Recipients who succumbed to donor-derived infection had higher inappropriate antibiotic use after infection, which emphasized the need of vigilant post-transplant clinical surveillance for timely and prompt targeted anti-infective prophylaxis or preemptive therapy in the event of donor-derived infection.

Conflict of interest

None declared.

- Alexander BD, Schell WA, Siston AM et al: Fatal Apophysomyces elegans infection transmitted by deceased donor renal allografts. Am J Transplant, 2010; 10: 2161–67
- 12. van der Vliet JA, Tidow G, Kootstra G et al: Transplantation of contaminated organs. Br J Surg, 1980; 67: 596–98
- Garrido J, Lerma JL, Heras M et al: Pseudoaneurysm of the iliac artery secondary to Aspergillus infection in two recipients of kidney transplants from the same donor. Am J Kidney Dis, 2003; 41: 488–92
- Vuruskan H, Ersoy A, Girgin NK et al: An unusual cause of ureteral obstruction in a renal transplant recipient: Ureteric aspergilloma. Transplant Proc, 2005; 37: 2115–17
- 15. Battaglia M, Ditonno P, Selvaggio O et al: Kidney transplants from infected donors: Our experience. Transplant Proc, 2004; 36: 491–92
- 16. Albano L, Bretagne S, Mamzer-Bruneel MF et al: Evidence that graft-site candidiasis after kidney transplantation is acquired during organ recovery: A multicenter study in France. Clin Infect Dis, 2009; 48: 194–202
- Garzoni C, Ison MG: Uniform definitions for donor-derived infectious disease transmissions in solid organ transplantation. Transplantation, 2011; 92: 1297–300
- Fishman JA, Greenwald MA, Grossi PA: Transmission of infection with human allografts: Essential considerations in donor screening. Clin Infect Dis, 2012; 55: 720–27
- 19. Gao F, Ye QF, Wan QQ et al: The distribution and resistance of pathogens among liver transplant recipients with *Acinetobacter baumannii* infections. Ther Clin Risk Manag, 2015; 11: 501–5
- 20. Wan Q, Ye Q, Zhou J: Mortality predictors of bloodstream infections in solid-organ transplant recipients. Exp Clin Transplant, 2013; 11: 211–14

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- 21. Kirchner VA, Pruett TL: Receiving the unwanted gift: Infection transmission through organ transplantation. Surg Infect (Larchmt), 2016; 17: 318–22
- Lonze BE, Dagher NN, Liu M et al: Outcomes of renal transplants from Centers for Disease Control and Prevention high-risk donors with prospective recipient viral testing: a single-center experience. Arch Surg, 2011; 146: 1261–66
- Helantera I, Salmela K, Kyllonen L et al: Pretransplant dialysis duration and risk of death after kidney transplantation in the current era. Transplantation, 2014; 98: 458–64
- 24. Goldberg E, Bishara J, Lev S et al: Organ transplantation from a donor colonized with a multidrug-resistant organism: A case report. Transpl Infect Dis, 2012; 14: 296–99
- 25. Gonzalez-Segura C, Pascual M, Garcia Huete L et al: Donors with positive blood culture: Could they transmit infections to the recipients? Transplant Proc, 2005; 37: 3664–66
- 26. Lumbreras C, Sanz F, Gonzalez A et al: Clinical significance of donor-unrecognized bacteremia in the outcome of solid-organ transplant recipients. Clin Infect Dis, 2001; 33: 722–26
- 27. Gupta RK, Gupta G, Chorasiya VK et al: Dengue virus transmission from living donor to recipient in liver transplantation: A case report. J Clin Exp Hepatol, 2016; 6: 59–61
- Green M, Covington S, Taranto S et al: Donor-derived transmission events in 2013: A Report of the Organ Procurement Transplant Network Ad Hoc Disease Transmission Advisory Committee. Transplantation, 2015; 99: 282–87

- 29. Kaul D, Dominguez N, Siparsky N et al: Time to presentation of donor derived infection. Presented at the American Transplant Congress. Seattle, WA. 2013. Am J Transplant, 2013; 13(Suppl. 5): Abstract B1038
- Altman DR, Sebra R, Hand J et al: Transmission of methicillin-resistant Staphylococcus aureus via deceased donor liver transplantation confirmed by whole genome sequencing. Am J Transplant, 2014; 14: 2640–44
- Johnston L, Chui L, Chang N et al: Cross-Canada spread of methicillin-resistant Staphylococcus aureus via transplant organs. Clin Infect Dis, 1999; 29: 819–23
- Wendt JM, Kaul D, Limbago BM et al: Transmission of methicillin-resistant Staphylococcus aureus infection through solid organ transplantation: Confirmation via whole genome sequencing. Am J Transplant, 2014; 14: 2633–39
- Len O, Garzoni C, Lumbreras C et al: Recommendations for screening of donor and recipient prior to solid organ transplantation and to minimize transmission of donor-derived infection. Clin Microbiol Infect, 2014; 20(Suppl. 7): 10–18
- 34. Gomez CA, Singh N: Donor-derived filamentous fungal infections in solid organ transplant recipients. Curr Opin Infect Dis, 2013, 26: 309–16
- 35. Mularoni A, Bertani A, Vizzini G et al: Outcome of transplantation using organs from donors infected or colonized with carbapenem-resistant gramnegative bacteria. Am J Transplant, 2015; 15: 2674–82
- 36. Lewis JD, Sifri CD: Multidrug-resistant bacterial donor-derived infection in solid organ transplantation. Curr Infect Dis Rep, 2016; 18: 18