


ORIGINAL ARTICLE

Successful repair of kidney graft artery rupture secondary to infection using a preprocessed homologous “Y”-shaped iliac artery

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Abstract

Objectives: This retrospective study aims to describe novel ways of repair kidney allograft artery rupture secondary to infection using a preprocessed homologous “Y”-shaped iliac artery.

Methods: Five patients' whose course was complicated by graft arterial rupture were included in the rupture group, and patients who received the kidney from the same donor were included in the control group. In the rupture group, the iliac artery used for revascularization was harvested from a DCD donor, pre-treated with absolute diethyl ether, followed by absolute alcohol, and then preserved in 75% alcohol. A biopsy of the arterial graft was obtained and stained using hematoxylin and eosin (H&E). Once a patient was diagnosed with kidney allograft arterial rupture by ultrasound, emergency surgery was conducted and the preprocessed “Y”-shaped iliac artery was used for bridging.

Results: Five patients were included in the rupture group. The “Y”-shaped iliac artery grafts were successfully preprocessed, H&E staining and electron microscope observation revealed few visible nuclei, with karyorrhexis and karyolysis. There were no significant differences in the long-term graft survival between two groups.

Conclusions: In conclusion, using preprocessed homologous “Y”-shaped iliac artery provides a useful method to bridge the vascular defects from kidney graft artery rupture secondary to infection in renal allograft recipients.

KEYWORDS

“Y”-shaped iliac artery, infection, kidney transplant

1 | INTRODUCTION

Kidney transplant is the optimal renal replacement therapy for patients with end-stage renal disease as it results in better quality of life and prolonged survival compared to hemodialysis or peritoneal

dialysis. Despite advances in surgical and immunosuppressive therapies, infection remains a major cause of morbidity and mortality in post-kidney transplantation patients.¹⁻⁵ Infectious arteritis leading to aneurysmal dilatation and renal artery rupture is a rare but potentially dangerous complication that occurs in fewer than 1% of patients,

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which can in some cases, result in life-threatening hemorrhage and need for transplant nephrectomy. Techniques for renal artery aneurysm repair include resection with tailoring, vein graft interposition, resection and reanastomosis, bypass, endovascular treatment with stents, and graftectomy. Unfortunately, graftectomy is the most frequently used technique in the cases reported due to the high risk of death for the patient in these cases.⁶⁻¹⁰ Under these circumstances, salvage of renal graft is very difficult. In our center, none of the renal grafts were successfully saved in cases of infection-induced artery damage until the experience described in this manuscript.¹¹ So, herein, we report our experience in successfully repairing five graft renal artery ruptures using preprocessed homologous "Y"-shaped iliac arteries for bridging after excision of the infected arteries.

2 | MATERIALS AND METHODS

2.1 | Patients

Patients who had kidney transplantation in our center and complicated with graft artery rupture secondary to infectious arteritis from January 2015 to December 2016 were included in the rupture group, and patients who received the kidney from the same donor who had not suffered artery rupture were included in the control group. Before operation, patients and their families were fully informed the risks of the replacement operation, and they have signed informed consent. All organs were recovered from the voluntary citizen-based organ donation system. The serum Cr levels before rupture, the highest after rupture, in rupture group and Cr levels in 6 months and 1 year after transplantation in both groups were recorded, and survival rate of patient/allograft of two groups was compared.

2.1.1 | Preprocess of vascular graft

The "Y"-shaped iliac artery was harvested from DCD donors, before donation, the family members of the donors have signed the informed consent for free donation of blood vessels, and it was approved by the ethics committee of the First Affiliated Hospital, College of Medicine, Zhejiang University. The adventitial layers were removed to allow the direct action of decellularization solutions on the medial and intimal vessel layers. Native vessels were treated in absolute diethyl ether for 24 hour, following a saline rinse. Vessels were transferred to absolute alcohol and treated for 72 hour and finally preserved in 75% alcohol for 4° refrigeration. The donor information and retention time were marked on the container.

Fresh samples and samples after absolute diethyl ether, and absolute alcohol were collected and stained using hematoxylin and eosin (H&E) and analyzed with electron microscope.

2.2 | Immunosuppression and antibiotics

The basic immunosuppressive regimen included induction with basiliximab or rabbit anti-human antithymocyte immunoglobulin (rATG) along with tacrolimus, MMF, and methylprednisolone. Basiliximab

was administered (20 mg/d) on the day of surgery and on postoperative day 4. rATG was started on the day of surgery (1.0 mg/kg/d for 5 days). Cyclosporine (5 mg/kg/d) or tacrolimus (0.1 mg/kg/d) was started along with MMF (2000 mg/d) on admission to maintain appropriate trough levels in blood. Methylprednisolone was administered according to our experience.

Protocol antibiotics included piperacillin tazobactam (4.5 mg q12h for 1 week) and caspofungin (50 mg/day for 1 week) if the culture of the donor was negative. Once donor cultures were available, antibiotics were tailored to the organism's sensitivity.

2.2.1 | Operation process

Once artery aneurysm was detected by computed tomography angiography or the active hemorrhage was detected by ultrasound after transplantation, an emergency operation was performed. First, the perirenal hematoma was cleared; blood flow of external iliac artery and vein were clamped by vascular clamps. The anastomotic suture was removed. The transplanted kidney was reperused with kidney preservation solution through the renal artery and covered with ice slush. We resected part of the renal artery close to the bifurcation and part of the recipient external iliac artery close to the anastomosis. Vascular continuity was re-established, using a preprocessed homologous "Y"-shaped iliac artery for

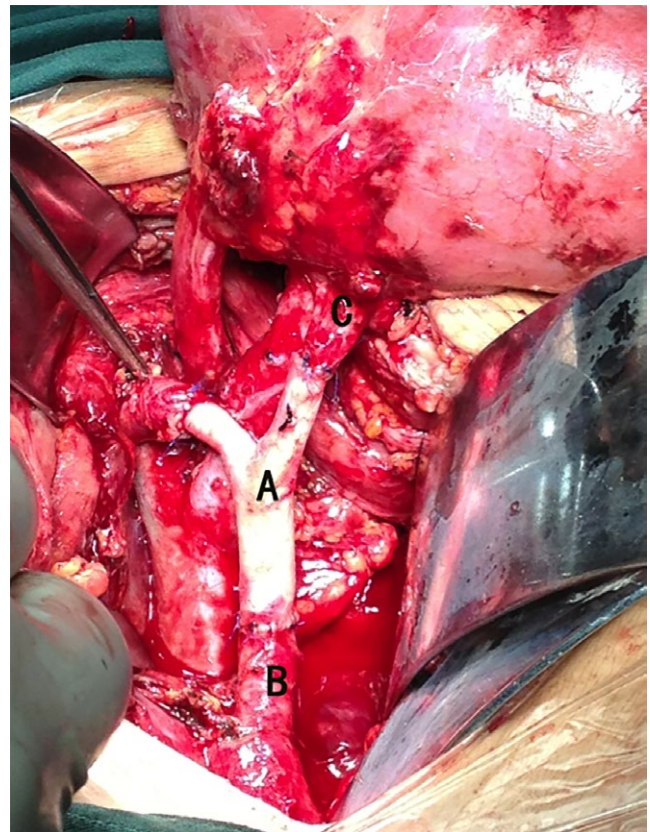


FIGURE 1 The picture of the arteries after bridging: preprocessed homologous "Y"-shaped iliac artery (A), external iliac artery (B), and renal artery (C)

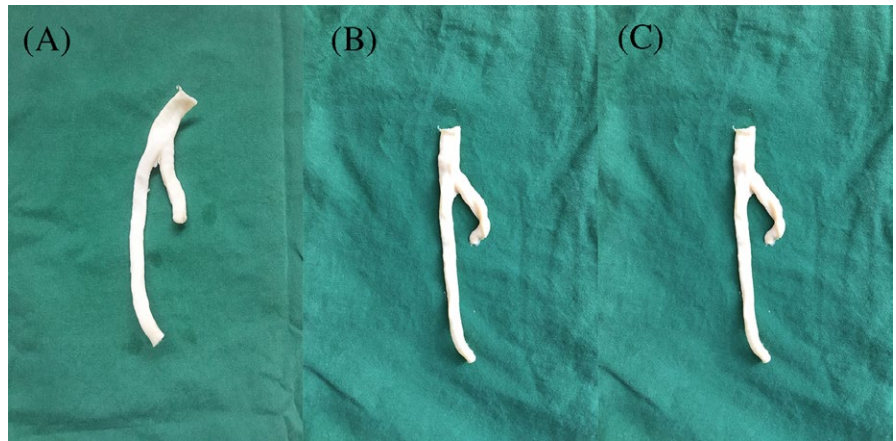


FIGURE 2 The picture of the arteries treated with absolute diethyl ether for 24 h (A), treated with absolute alcohol for 72 h (B) and preserved in 75% alcohol for several weeks (C)

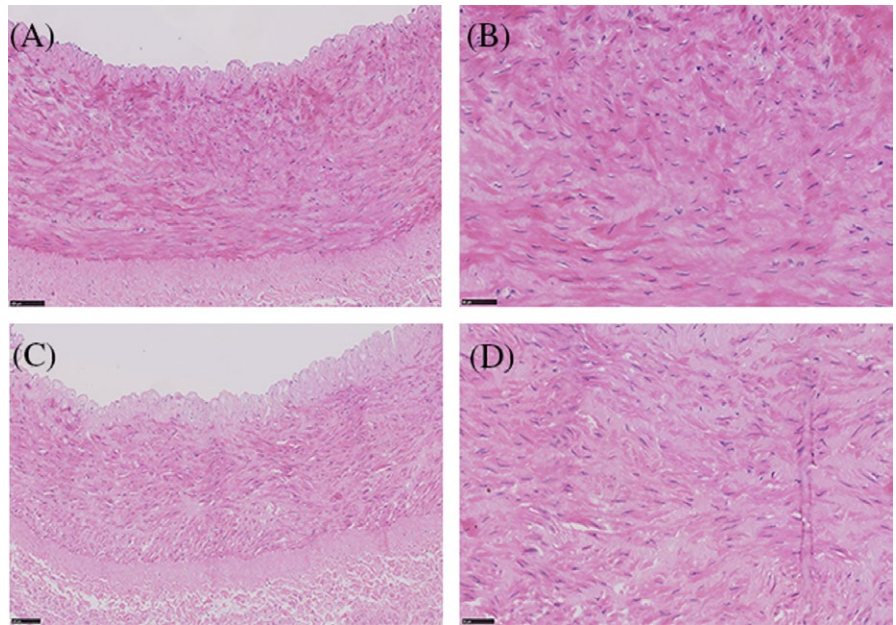


FIGURE 3 H&E staining of iliac arteries before decellularization (A) and after absolute diethyl and absolute alcohol (C). Scale bar: 100 μ m. H&E staining of iliac arteries before decellularization (B) and after absolute diethyl and absolute alcohol (D). Scale bar: 50 μ m

bridging (Figure 1). The preprocessed homologous “Y”-shaped iliac artery needed to be fully rinsed with saline and the branch should be ligated before use. The graft regained blood flow after bridging, and the ischemic time was recorded. The blood clot and resected artery were sent for etiological examination. After surgery, effective antibiotics were administered according to culture result.

2.3 | Statistical analysis

The quantitative variables were presented as means \pm SEM, the Student's *t* test was used for quantitative variables. *P* value <0.05 was considered as significant. Analyses were performed using SPSS 23.0 (Armonk, NY, USA).

3 | RESULTS

3.1 | Histologic evaluation of arteries

Fresh vessel and vessels after continuous treatment are shown in Figure 2. Gradually, the vessel became inflexible and thin. H&E

staining of vessels that were exposed to treatment revealed few visually detectable nuclei, and vessels were dilated as compared to fresh sample and wall thick were reduced (Figure 3). Under electron microscopy, many nuclei have undergone karyorrhexis and karyolysis and the endothelial cell have adrift from medial vessel layers while the elastic fibers remained (Figure 4).

3.2 | Patients and clinical outcomes

A total of 910 consecutive patients underwent kidney transplant (KT) at our center from January 2015 to December 2016. There were 340 cases (37.4%) of living KTs and 570 cases (62.6%) of deceased KTs. Five patients (0.5%) suffered graft artery rupture; all from deceased donors. Table 1 showed demographic data of the two groups: the rupture group (mean age, 54.8 ± 7.7 ; range, 43–61 years; 4 males) and the control group (mean age, 53.0 ± 9.1 ; range, 44–64 years; 3 males). The age of the blood vessel donors was 42.2 ± 6.8 years. The primary kidney diseases of the rupture group were chronic glomerulonephritis ($n = 2$), IgA nephropathy ($n = 2$), and polycystic

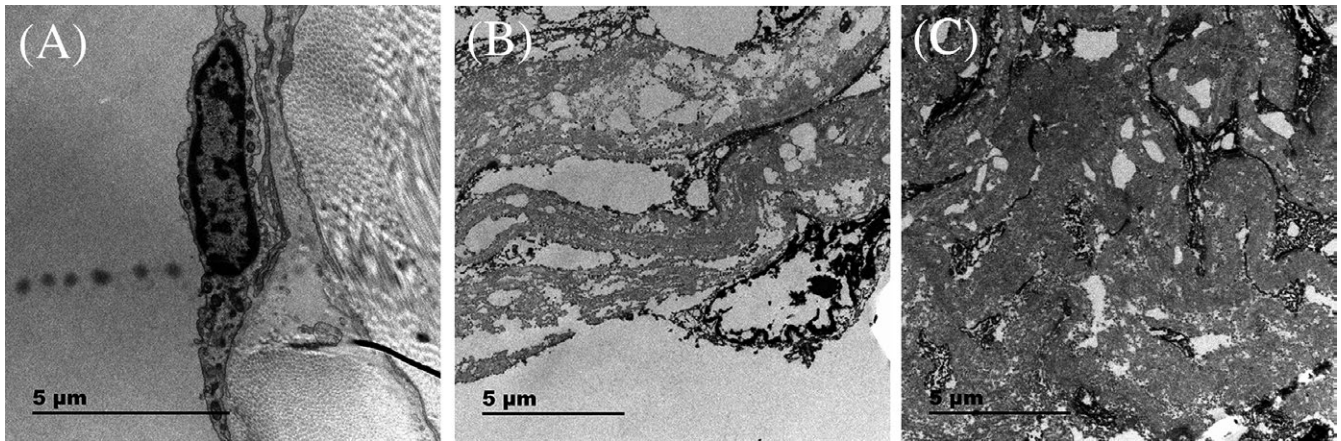


FIGURE 4 Under electron microscopy, the intact endothelial cell (A). After the treatment nuclei have undergone karyorrhexis and karyolysis and the endothelial cell have adrift from medial vessel layers (B), the elastic fibers remained well (C). Scale bar: 5 μ m

kidney (n = 1), and in the control group, there were chronic glomerulonephritis (n = 3), IgA nephropathy (n = 1), and Diabetic nephropathy (n = 1). In the rupture group, three patients were under maintenance hemodialysis while two patients under peritoneal dialysis, and in the control group, four patients were under maintenance hemodialysis while one patient under peritoneal dialysis before transplantation. The basic immunosuppressive agents all were tacrolimus, and the induction therapy were Basiliximab (n = 3) and rATG (n = 2) in both groups. The rupture of renal artery happened at

a mean of 12.8 ± 4.7 days; range 9-21 after the transplantation. The re-ischemia time was 40.6 ± 3.2 minute.

Before the repair operation, two patients complained of abdominal pain and with the marked decrease of hemoglobin were diagnosed with graft artery aneurysm formation and active hemorrhage by computed tomography angiography (CTA), three patients were diagnosed active hemorrhage visualized by ultrasound and had signs of hypovolemic, hemorrhagic shock, and CTA is not allowed in case of emergency. All five patients underwent emergency operation. As confirmed by imaging, graft artery aneurysm was confirmed in two patients and graft artery rupture was detected in the other three patients.

The culture results of donor/recipient of the five cases are listed in Table 2.

The pathogenic bacteria were *Acinetobacter baumannii* (n = 2), which was positive in donor sputum, kidney preservation solution, drainage, and blood clot cultures; *Candida albicans* (n = 1), which was positive in kidney preservation solution, drainage, and blood clot cultures; *Candida tropicalis* (n = 1), which was positive in kidney preservation solution, drainage, and blood clot cultures; and *Staphylococcus epidermidis* (n = 1), which was positive in drainage and blood clot cultures. The presence of fungi in the ruptured graft artery of 2 patients was confirmed by histological examination (Figure 5). Broad spectrum antibiotics were initiated after the surgery, then switched to sensitive antibiotics according to the culture results. The detailed antibiotic therapy is listed in Table 3.

The survival rate of patient/allograft of two groups was 100% at 1 year after bypass surgery. Acute rejection, ureteral complications, and BK virus infection did not occur during the whole follow-up period in both groups. In the rupture group, serum Cr was significantly elevated after rupture (1.46 ± 0.32 mg/dL before, 2.48 ± 1.34 mg/dL peak post rupture, $P < 0.01$). One week after the replacement surgery, the serum Cr quickly decreased to 1.37 ± 0.61 mg/dL, and 6 months and 1 year later, the mean serum Cr was 1.16 ± 0.43 mg/dL and 1.13 ± 0.34 mg/d, respectively ($P > 0.05$ for all, compared with Cr before rupture). In control group, the mean serum Cr of 1 week,

TABLE 1 Summary of the five cases of rupture of the renal artery

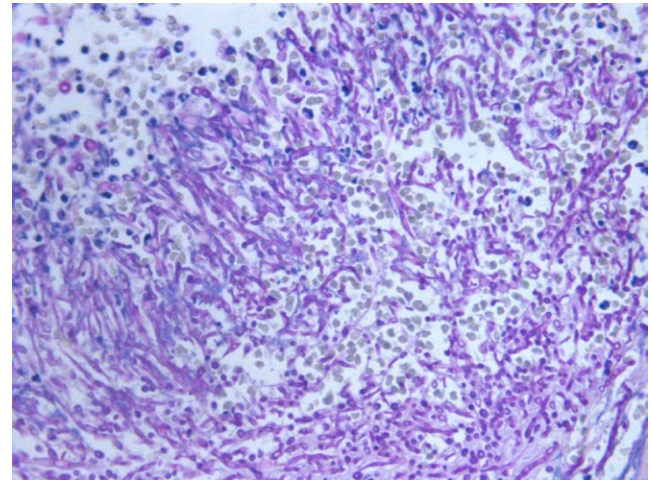
| Variable | Rupture group | Control group |
|---|----------------|---------------|
| Sex, n (%) | | |
| Male | 4 (80%) | 3 (60%) |
| Female | 1 (20%) | 2 (40%) |
| Mean age, years (range) | 54.8 (43-61) | 53.0 (44-60) |
| Cause of ESRD, n(%) | | |
| Chronic glomerulonephritis | 2 (40%) | 3 (60%) |
| IgA nephropathy | 2 (40%) | 1 (20%) |
| Polycystic kidney | 1 (20%) | 0 |
| Diabetic nephropathy | 0 | 1 (20%) |
| Dialysis, n (%) | | |
| HD | 3 (60%) | 4 (80%) |
| PD | 2 (40%) | 1 (20%) |
| Induction therapy, n (%) | | |
| Basiliximab | 3 (60%) | 3 (60%) |
| rATG | 2 (40%) | 2 (40%) |
| Rupture time (days after transplantation) | 12.8 (9-21) | — |
| ischemic time(min) | 40.6 ± 3.2 | — |

ESRD, end-stage renal disease; HD, hemodialysis; PD, peritoneal dialysis

TABLE 2 The culture results of donor/recipient of the five cases

| | Donor | | | | Recipient | | | | |
|-----------|---------------|---------------|--------------------|--------------------------------------|---------------|---------------|--------------------|--------------------|--|
| | Blood culture | Urine culture | Sputum culture | Kidney preservation solution culture | Blood culture | Urine culture | Drainage culture | Blood clot culture | |
| Patient 1 | N | N | <i>A baumannii</i> | <i>A baumannii</i> | N | N | <i>A baumannii</i> | <i>A baumannii</i> | |
| Patient 2 | N | N | N | CA | N | N | CA | CA | |
| Patient 3 | N | N | <i>A baumannii</i> | <i>A baumannii</i> | N | N | <i>A baumannii</i> | <i>A baumannii</i> | |
| Patient 4 | N | N | N | N | N | N | SE | SE | |
| Patient 5 | N | N | N | CT | N | N | CT | CT | |

CA: *Candida albicans*; CT: *Candida tropicalis*; N: negative; SE: *Staphylococcus epidermidis*.

**FIGURE 5** Photomicrograph of the tubular septate branching hyphae flooding the ruptured artery (PAS, original magnification $\times 40$)

6 months, and 1 year after the transplantation was 1.85 ± 0.85 mg/dL, 1.25 ± 0.09 mg/dL, and 1.28 ± 0.10 mg/dL, respectively, and there were no significant differences between two groups (Figure 6).

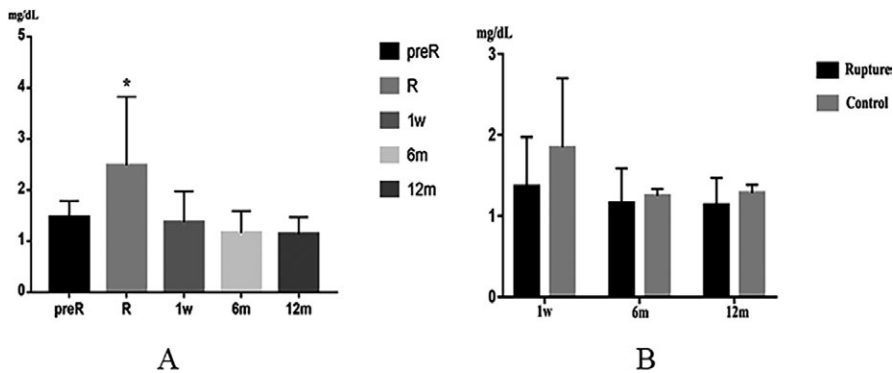
About 6 months after replacement surgery, five patients in rupture group underwent computed tomography angiography. The CT scan showed that blood flow through the transplanted arteries was normal.

4 | DISCUSSION

In this paper, we presented a new method of repair kidney graft artery rupture secondary to infection using a preprocessed homologous “Y”-shaped iliac artery. The preprocessed homologous “Y”-shaped iliac artery was harvested with the organs from the DCD donor and treated with absolute diethyl ether and absolute alcohol then preserved in 75% alcohol. After the treatment, the vessels revealed few visually detectable nuclei and many nuclei have undergone karyorrhexis and karyolysis, while the elastic fibers remained and acted as a vascular stent. In this study, effectiveness of the decellularization techniques was confirmed according to the methods have been reported elsewhere.^{12,13} We successfully saved the kidney grafts using these preprocessed homologous “Y”-shaped iliac arteries for bridging after excision of the infectious arteries. After surgery, effective antibiotics were administered according to microbiologic sensitivity. The serum Cr of the five patients presented transient elevation and returned to normal soon. In our center, this is the first time we successfully saved kidney grafts from arterial infection and rupture.

Vascular infection is an infrequent but serious complication of organ transplantation. In France, the estimated incidence of *Candida* graft site infection was 1 case per 1000 grafts.⁴ In our center, the rate of aspergillosis was 0.5% according to a report by Wang et al.¹¹ The DCD donors often were treated in the ICU for several days before organ extraction, and it is known that vascular infections may

| | Pathogen | Antibiotics | Course |
|-----------|-----------------------------------|-------------------------------|--|
| Patient 1 | <i>Acinetobacter baumannii</i> | Tigecycline, sulbactam sodium | 2 wk |
| Patient 2 | <i>Candida albicans</i> | Caspofungin, fluconazole | Caspofungin (2 wk), fluconazole (3 mo) |
| Patient 3 | <i>Acinetobacter baumannii</i> | Tigecycline, sulbactam sodium | 4 wk |
| Patient 4 | <i>Staphylococcus epidermidis</i> | Tigecycline | 2 ws |
| Patient 5 | <i>Candida tropicalis</i> | Voriconazole, posaconazole | Voriconazole (2 wk), posaconazole (3 mo) |

TABLE 3 The pathogens and the antibiotic treatment of the five cases

FIGURE 6 In rupture group, serum Cr was significantly elevated after rupture ($P < 0.01$), and the serum Cr quickly decreased to normal in one week after the bridging surgery (A). There were no significant differences in mean serum Cr of 1 wk, 6 mo, and 1 y after the transplantation between two groups (B).

be more likely to occur in recipients whose donors have spent prolonged periods in the ICU (more than 7 days).²

Of the few reports in the English literature involving graft rescue in cases of infection-induced artery damage, saving the affected recipient's graft and artery is often difficult to achieve.⁶⁻⁸ Albano et al⁴ reported the cases of two patients with aneurysms of the iliac artery caused by *Candida* arteritis in which the graft was saved after arterial patching. Osman et al¹⁴ analyzed the data from 24 patients with pseudoaneurysms related to kidney grafts. Only five of the grafts (21%) were saved, while 9 of 17 patients lost the iliac or femoral artery, with or without subsequent bypass. Kaabak et al¹⁵ successfully repaired artery rupture associated with a kidney graft using external stenting, while Minz et al¹⁶ used autogenous internal iliac artery to bridge the external iliac artery after excision of *Aspergillus* mycotic aneurysms in renal transplant recipients.

In the past before the widespread use of synthetic grafts, biological grafts were used for vascular access and peripheral bypass surgery. Xenografts, including natural bovine tissues (carotid artery and visceral veins), have been used for hemodialysis access. Cryopreserved vascular allograft tissue has been shown to be useful in difficult vascular access situations. Cryopreserved vascular tissue is effective in cases of active infection and can be placed directly in the infected field with a low recurrence of infection.¹⁷⁻¹⁹ In a cohort study of patients who received arteriovenous grafts, primary and primary assisted patencies were similar between bovine carotid artery (BCA) biologic graft and expanded polytetrafluoroethylene (ePTFE). However, secondary patency was higher for BCA,

indicating better durability for the biologic graft than for ePTFE grafts.²⁰ In our center, the preprocessed artery was first used as vascular access for arteriovenous internal fistula, and from this experience, we decided to use it to save the kidney graft for bridging after attempt the failure of simply repair and arterial patching.

To our knowledge, this is the first report of a technique using a preprocessed homologous "Y"-shaped iliac artery in such settings in the English literature. Using such an artery for bridging has many advantages. First, the "Y"-shaped artery is a good match for the external iliac artery and the transplanted kidney artery. Second, we were able to excise as much as possible of the infected artery in order to remove any remaining pathogenic organisms. Third, the artery was preserved in 75% alcohol and can be used when needed.

Early recognition of vascular infection is very important and dependent on a high index of suspicion, early use of diagnostic procedures, and knowledge of the possible spectrum of organisms together with early intervention by appropriate surgical and aggressive antimicrobial therapy, because it can lead to life-threatening hemorrhage and a need for transplant nephrectomy. Infection may already be present in the donor, or can occur by contamination of the organ during harvest, preservation, and handling, or at transplantation. The results of two cases of donor sputum, kidney preservation solution, drainage, and blood clot culture were *Acinetobacter baumannii* suggesting that the infection was delivered from donor. The other three cases may be infected by other ways. Therefore, effective antibiotics should be administered to a recipient based on the results of culture of samples from donor and recipient.

We acknowledge that this study is limited by the retrospective design, small sample size and follow-up is relatively short. Although all five cases were successfully treated, we still have some doubts. The patients in control group used the similar immunosuppression regimen and prophylactic antibiotics as in the rupture group, but why they didn't develop severe infection and eventually renal graft artery rupture? Most of the cases reported in the literature also occurred in only one recipient. Is it because of the difference in the physical condition of the recipient, the difference in the number of bacteria entering the recipient, or the difference in the sensitivity of the recipient to antibiotics? Because the number of such cases is too small, it is difficult to find out the answers at the moment. The cryopreserved vascular tissue was effective in cases of active infection and can be placed directly in the infected field, does our preprocessed homologous "Y"-shaped iliac artery have similar effects? It leaves room for further investigation in a larger cohort of cases. Despite these limitations, it was a successful and ambitious attempt.

In conclusion, using preprocessed homologous "Y"-shaped iliac artery provides a good addition to the transplant surgeon's armamentarium, which provides a useful method to bridge the vascular defects created by radical debridement in presence of infections in renal allograft recipients.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHORS' CONTRIBUTIONS

Dr Jianghua Chen designed this work. Guangjun Liu was the main writer of the manuscript. Xuliang Wang concentrated on organizing and analyzing the data. Jianyong Wu, Wenhan Peng, Rending Wang and Hongfeng Huang were the surgeons of the patients.

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