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Original Article

A case of kidney transplantation using donation after circulatory death with renal calculi

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Abstract: Donation after circulatory death (DCD) supplies a big percentage of the organ source pool. Compared to living-related donations, donor kidneys from DCD are commonly with lower quality since they inevitably suffer from hypoxia, hypotension, and inadequate organ perfusion during the progression to circulatory arrest. The current case presents a 44-year-old male donor with wide range subarachnoid hemorrhage and multiple skull fracture from a car accident. Multiple stones were detected in his right kidney. We performed a modified *ex vivo*pyelolithotomy and ureteroscopy on the bench to render a stone-free allograft. We also improved the donor kidney with hypothermic/perfusion preservation machine before renal transplantation. The recipient showed no complications during the first two-month post-operational follow-up. Such a donor kidney with stones may probably be discarded by conventional perspective. Yet, the combination of the *ex vivo* bench-surgery technique and hypothermic oxygenation/perfusion makes it a qualified donor kidney. Thus we have demonstrated a promising way of saving borderline qualified DCD donor kidneys.

Keywords: Donation after circulatory death, kidney transplantation, pyelolithotomy, ureteroscopy, renal calculi

Introduction

Due to the limited amount of living-related donations, donations after circulatory death (DCD) are the major source for solid organ transplantation worldwide. In kidney transplantation, strategies aiming to increase the number of usable DCD organs are widely used [1]. However, kidneys need special surgical procedures such as those with kidney stones are not commonly applicable.

A recent epidemiological study shows that the upper urinary tract stone including kidney stone has an age adjusted prevalence at 7.38% in China [2]. Given the huge population, potential DCD donor kidneys with stones won't be rare. A quick decision must be made by transplant surgeon, when confronted with such cases-discard or use? Guidelines in the literature for DCD donor's kidney with calculi are mostly descriptive or not specific. Here we reported a successful application of the *ex vivo* bench-surgery technique and hypothermic oxygenation/perfusion to generate a qualified donor kidney from a DCD donor with kidney stone, and performed a successful kidney transplantation.

Case report

The nephrolithiasis kidney was carried by a 44-year-old male who was admitted to the emergency room due to head-injury-cause-unconsciousness in a car accident. Wide range subarachnoid hemorrhage and multiple skull fracture were fatal. Radiographs of the chest and abdomen showed no fractures or other acute processes. However, multiple renal calculi and one pyeloureteric junctional stone (PUJ) were found in the right kidney (**Figure 1**). Next of kin reached consensus to DCD after being informed that the patient had tiny chance to recover and basically was brain dead. Last vital signs before withdrawal of life support were blood pressure at 95/56 mmHg, pulse rate at 140 beats/min and oxygen saturation at 98%.

Based on the categories of non-heart-beating donors, this is a Maastricht classification 3 case [3, 4]. Organs were perfused *in situ* with

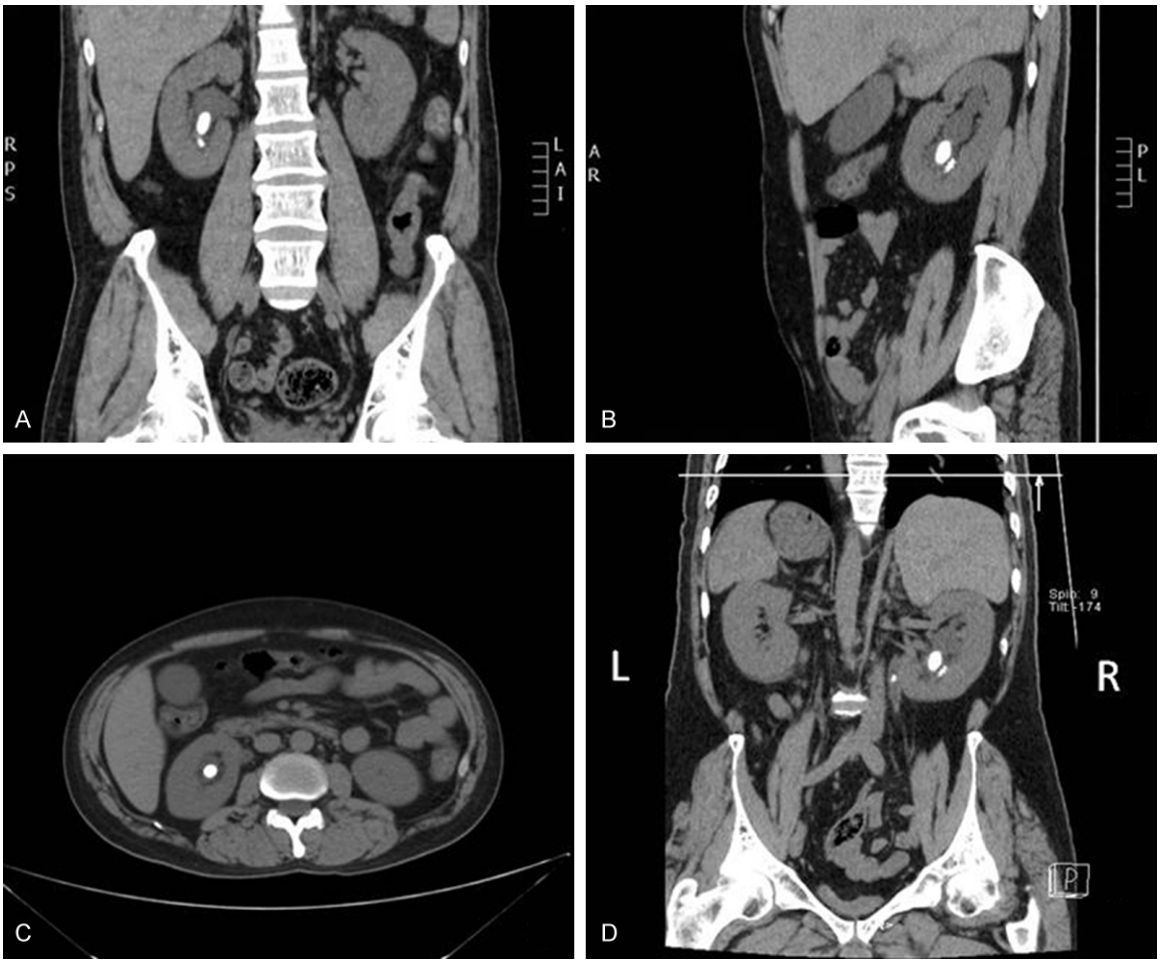

Figure 1. Location and size of the donor kidney calculi. (A) Coronal plane image shows that the lower calyx deposits 2 large visible stones. And the major axis is 18 mm long. (B) Sagittal plane focus on the same spot as (A). (C) Horizontal scanning is aiming at the major axis. (D) This is a reconstructed image that allows us to have a visual on all significant stones.

University of Wisconsin (UW) solution during open surgery. The isolated donor kidney was delivered to the prepared back-table or "bench" and was immersed in ice-slush. Palpation on the upper ureter, the stone was confirmed as found by the CT. Considering the presence of major lower calyces stones and the ureteral calculi, a routine ureteroscopy performed via the ureteral stump would not be suitable [5]. Therefore a modified surgical approach was performed. We made a 1.5-cm-incision along the ureter superior to the palpable stone site (Supplementary Figure 1A). A blind-exploratory attempt for the ureteral calculi with mosquito forcep was successful and the stone was pulled out intact. A 7.5-F rigid ureteroscope was used for systemic calyx inspection and the identified stones were removed with forcep-assist fragmentation and zero-tip basket extraction. Subsequently, we flush the kidney with a 6-F catheter through the incision gaining pressure from a syringe-push to clear dust and particles (Supplementary Figure 1B). All procedure took about 20 minutes. Following the bench-surgery, the kidney was applied for hypothermic machine perfusion with LifePort (Organ Recovery Systems, Itasca, IL, USA). Mean pressure was set at 30 mmHg in pulsatile mode. Specific values of the machine indexes are shown in Supplementary Figure 2. Transplantation was performed using standard extraperitoneal technique with vascular anastomosis to the external iliac vein and iliac artery. A 7-F 16-cm transplant double-J stent was placed and removed 5 weeks after surgery.

The patient's recovery and the morphology/function of the transplanted kidney were monitored. One week post-transplantation ultrasonography demonstrated a fine blood flow of the

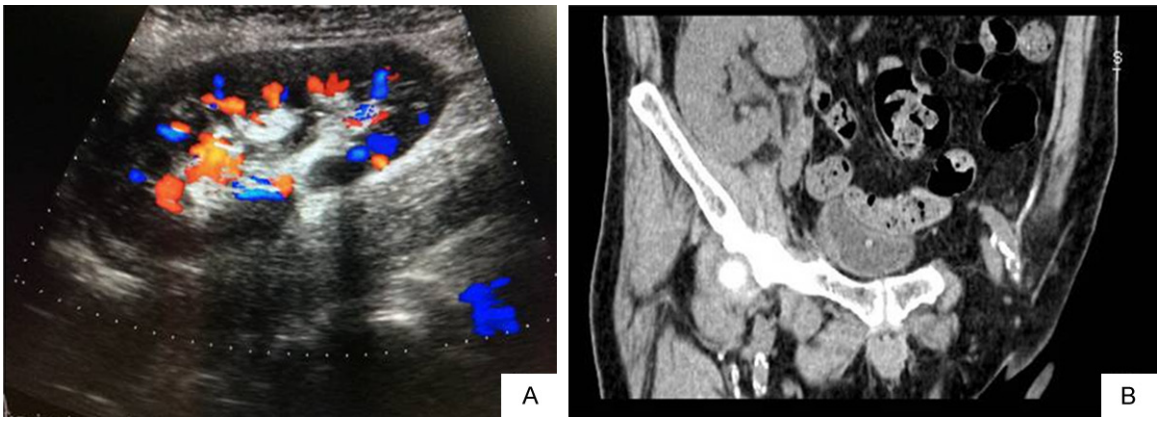

Figure 2. Allograft in recipient. A. One-week post-transplant Color Doppler ultrasound suggests a fine blood supply, though accompanied with strong echo in collecting system. B. Five weeks post-surgery CT on the recipient demonstrates a morphological well-being and stone-free kidney.

grafted kidney (**Figure 2A**). Meanwhile, collecting system strong echo indicated debris of the fragmentation. Further follow-up observation revealed a declining intensity of the intra-collecting-system strong echo. Abdominal CT scan revealed no major abnormality at five weeks after transplantation (**Figure 2B**). Serum creatinine and blood urea nitrogen were rehabilitated (Supplementary Figure 1C). No delayed graft function (DGF) or other complications were detected during the observational follow-up.

Discussion

Since the gap between organ supply and demand has not been narrowed significantly, the need for specific and sensitive surrogates of organ source is becoming even more critical. Kidneys of "uncertain" quality originating from extended criteria donors (ECDs) or DCD are increasingly used. These kidneys have a higher incidence of primary nonfunction (PNF) or delayed graft function (DGF) compared with standard criteria donor (SCD) kidneys [6, 7]. A DCD donor inevitably suffers from hypoxia, hypotension, and inadequate organ perfusion during the progression to circulatory arrest [8], which might play a critical role in PNF and DGF.

Urolithiasis is common in potential DCD donors. Such a donor kidney with stones may probably be discarded by conventional perspective. There were some living donor's precedents in the literature reporting renal calculi can be successfully retrieved during living-related transplantation at the time of transplant itself using endourological methodology of *ex vivo* ureteroscopy [9, 10]. The fact was all these donors were asymptomatic and under close pre-surgery check-up. Presumed risk of donor morbidity from possible stone formation in the solitary remaining kidney and potential recipient morbidity from obstruction attributable to "donor-gifted" stone could be manageable.

Not like living kidney donors mentioned above, precise history of disease and evaluations like glomerular filtration rate and intravenous pyelography cannot be obtained in full version. DCD-condition-induced-injury factors, compared to living donors, may attribute to ischemia-reperfusion injury more seriously. Ischemia in general, whether warm or cold, causes graft injury by several mechanisms. First of all, depletion of cellular energy stores leads to inhibition of membrane transport systems, which in turn causes intracellular accumulation of ions and water resulting in cell swelling. Second, reperfusion injury becomes manifest through up-regulation and surface expression of adhesion molecules, which activate host leukocytes. By binding to the endothelium and releasing oxygen free radicals and inflammatory mediators, polymorphonuclear leukocytes will contribute to vascular injury. Third, cytokine released by infiltrated lymphocytes and macrophages may trigger allograft immunogenicity, rendering the organ more susceptible to a host immune attack.

Strategies aiming to increase the number of viable DCD organs such as extension of the waiting time to circulatory, re-evaluation of timing and/or declaration of death and increased

use of pediatric DCD organs transplanted to adult and pediatric recipients as recommended [1] are being practiced worldwide. With blurry pre-transplant assessment and unexpected kidney stone, the viability of the donor kidney cannot be assured. However, by combining hypothermic oxygenation/perfusion and *ex vivo* bench-surgery technique, we successfully evaluate and improve the donor kidney simultaneously.

Ischemia-reperfusion injury is believed to occur at the time of warm oxygenated recirculation and not during ischemic storage. However, if cold stored organs are first exposed to oxygen under hypothermic conditions, and subsequently warm reperfused, the degree of injury is lower. Hypothermic oxygenation/perfusion is more optimal than static cold storage for the deceased donor kidney. With a short period of hypothermic oxygenation, the function and one-year survival rate of the graft is improved [11]. Mechanistically, oxygenation under hypothermic conditions protects the kidney from mitochondrial and nuclear injury by down-regulation of mitochondrial activity before reperfusion. Also, cold perfusion itself, under low pressure conditions, prevents endothelial damage, independently of oxygen [12].

Bench surgery describes reconstructive surgery on diseased kidneys receiving asanguineous perfusion outside the body was coined by Guerriero, Scott, and Joyce [13]. This type of surgical intervention provides advantages such as less ischemic time, operation space, kidney rotation availability. Jonathon et al. [10] conducted a retrospective study on 17 living kidney donors with renal stones (range 2-12 mm) screened out from 377 potential donors via CT were proceeded to *ex vivo*ureteroscopy (ExURS) on the bench. Basket retrieval and laser fragmentation technique were used. Vasdev et al. [9] reported 2 cases of ureteroscopic removal of small stones (range 3-5 mm) with a basket. The procedure was carried out after the kidney was revascularized in the recipient before the ureterovesical anastomosis. Devasia et al. [14] removed a 15-mm stone at the time of transplantation using nephrolithotomy with assistant of ultrasonography. No bad outcomes were reported for all the recipients and donors recruited in these studies.

In our case, the largest stone was 18 mm and was located in the lower calyx. In addition, a 5-mm stone was obstructing the PUJ. This specific condition is not suitable to adopt simple ExURS through the stump. Besides ureteroscope-induced distal ureter injury might compromise ureter end blood supply which is the most common reason for hydronephrosis of the allograft kidney. Therefore, we made an incision to avoid bad prognosis and ease the operational difficulty.

In conclusion, the introduction of hypothermic oxygenation/perfusion and *ex vivo*ureteroscopic management using the flexible ureteroscope and mosquito forcep blind-explore fragmentation is safe, successful, and associated with no short-term graft-related complications or urological complications.

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Disclosure of conflict of interest

None.

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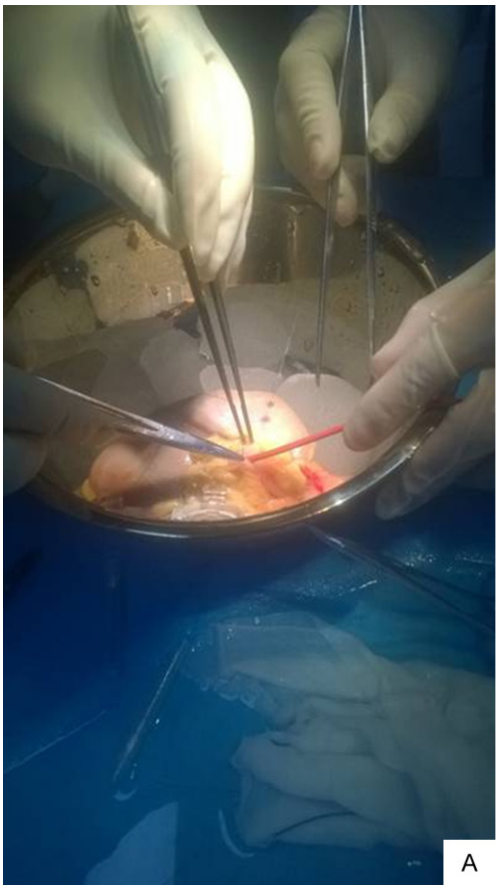
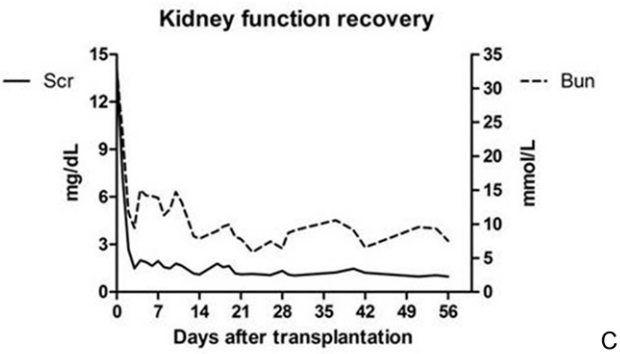


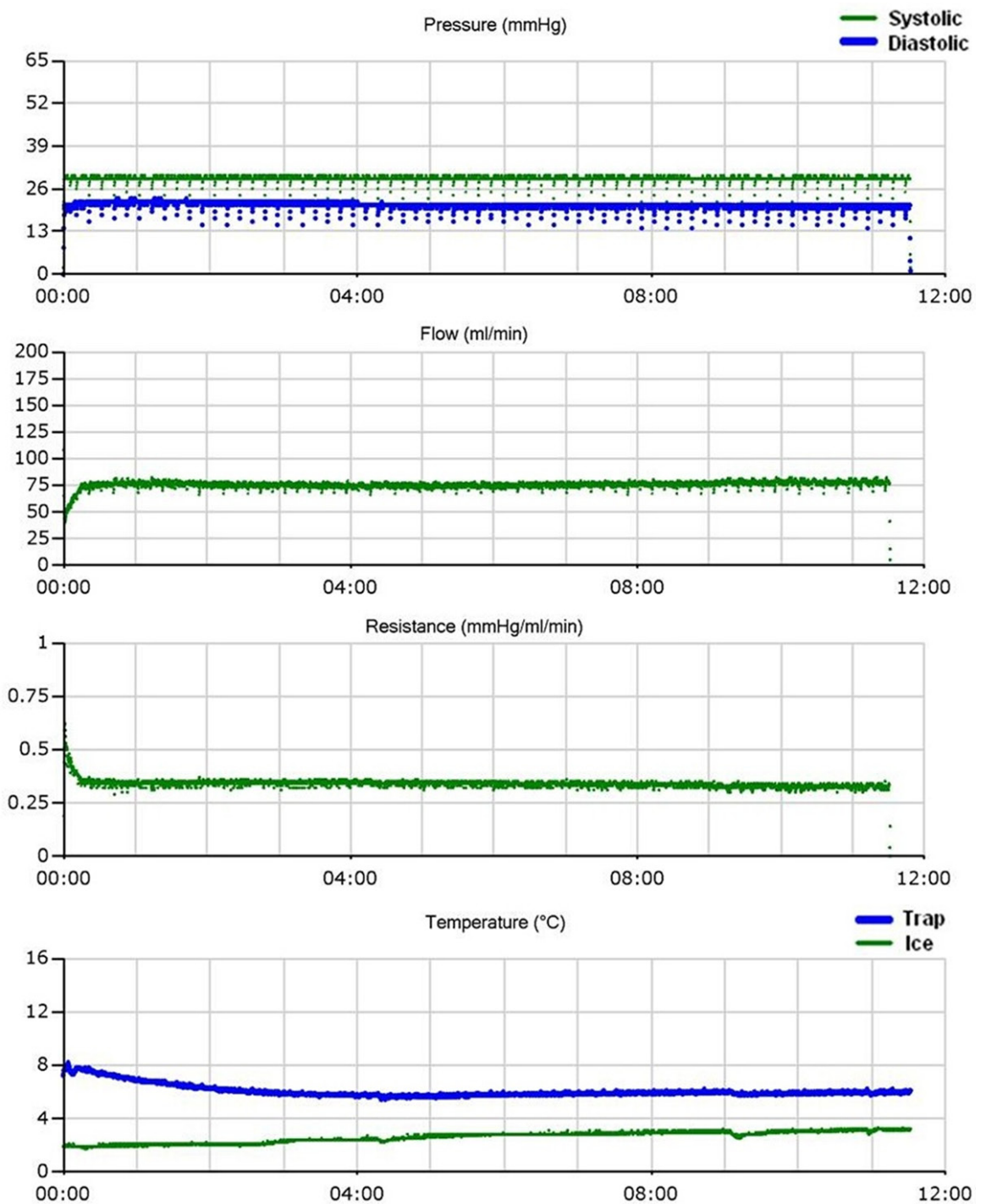
A

B



C

Supplementary Figure 1. A. Flushing the fragmentation debris through the 1.5-cm-incision. B. Part of the stone fragments. C. Abbreviations, Scr, serum creatine; Bun, Blood urea nitrogen. Sudden drop can be observed in the first 3 days. Scr was plotted on the left Y axis; Bun was depicted on the right Y axis.



Supplementary Figure 2. Machine indexes. Such a performance of the donor kidney indicates good quality and prognosis.