Original Research Article

Ex-Vivo Management of Renal Calculi in Living Donor Kidneys: A Retrospective study from Malaysia

Abstract:
Renal transplantation has significantly improved outcomes for patients with End Stage Renal Disease (ESRD), with living kidney donors offering advantages such as better long-term survival and immediate graft function. However, the presence of renal stones in potential living donors has historically been a contraindication for transplantation due to the risks it poses to both the recipient and the donor. The objective of the study is to evaluate the feasibility and safety of ex-vivo management of renal calculi in living donor kidneys and its potential impact on the transplantation process. This retrospective study from Malaysia describes the ex-vivo management of renal calculi in living donor kidneys prior to transplantation, aiming to expedite the transplantation process for recipients in urgent need.
A total of four living donors with incidental non-obstructing renal stones underwent ex-vivo surgery at University Malaya Medical Centre. Preoperative evaluations and risk stratification were performed to ensure the well-being of the remaining kidney. Intraoperatively, flexible uretero-renoscopy (URS) was used to visualize the collecting system of the graft kidney. In one case, the stone was successfully removed using a stone basket, while in the remaining cases, no stones were found, and the radio-opacity seen in preoperative imaging was identified as benign Randall's plaques.
No immediate complications or compromise in early graft function were observed. Both donors and recipients remained well during the follow-up period, with no occurrences of urolithiasis. The ex-vivo procedure added minimal cold ischemia time to the transplantation process, allowing quick access to the collecting system while being cautious not to injure the ureter.
In conclusion, ex-vivo management of renal stones in living donor kidneys represents a potential solution to expand the pool of suitable organs for transplantation. However, the optimal operative management of graft urolithiasis remains debatable, and individualized assessment and multidisciplinary team discussions are necessary to ensure safety and success.
Long-term follow-up and larger studies are required to evaluate the impact of this technique on graft function and outcomes.

Keywords: Ex-vivo uretero-renoscopy(URS); extracorporeal bench surgery; living donor renal graft; renal calculus; transplant

Introduction

Renal transplantation in the setting of End Stage Renal Disease (ESRD) has paved a new outlook in the outcome of this debilitating condition. The responses from the national cadaveric transplant program have yet to gain acceptance from society in our country. Living kidney-donors provide the added advantage of improved long-term survival, immediate functioning of the graft, better graft survival, and the option of a pre-emptive transplant as compared to deceased donors[1,2]. To address the issue of organ shortage, many centres around the world, including University Malaya Medical Centre(UMMC), have adopted expanded criteria for donor selection, which includes donors with asymptomatic renal stone.[3]

Historically, patients with renal stones have been excluded from transplantation in many institutions[4]. Stones in the upper tract could pose a threat to the recipient with the potential complications of oliguria, hematuria, and rising creatinine[5]. While donors carry the added risk of future stone formation, with the possibility of obstructive uropathy and progression to end stage renal disease(ESRD)[6].

There are several options available for the management of the stone-bearing kidney. They were either treated before the donor-nephrectomy, ex-vivo surgery at the time of transplantation or transplanted with the stone in-situ with an intention for a deferred intervention.[6] Adopting an ex-vivo approach for renal stone management can expedite the transplantation process as compared to pre-transplant stone clearance in the donor-gifted kidney. This is important especially for recipients in urgent need of transplantation as an alternative to dialysis. However, feasibility and safety of ex-vivo management of renal calculi in living donor kidneys and its potential impact on the transplantation process as well as the optimal operative management for such patients is still under debate. We report our experience and the short-term outcomes of living donor kidney with renal calculi. This would be the first retrospective study from Malaysia on ex-vivo stone management in living donor kidney prior to transplantation.

Objectives

The objective of the study is to evaluate the feasibility and safety of ex-vivo management of renal calculi in living donor kidneys and its potential impact on the transplantation process. The study aims to assess the outcomes of this procedure, including the successful removal of renal stones, the absence of complications or compromise in early graft function, and the absence of urolithiasis in both donors and recipients during the follow-up period. Additionally, the study aims to highlight the potential benefits of ex-vivo surgery in expanding the pool of suitable organs for transplantation and to generate insights that can contribute to the ongoing discussion on the optimal operative management of graft urolithiasis. The long-term impact on graft function and outcomes will also be explored.

Methods

Conventional pre-transplant evaluation of potential donors in living related renal transplant program at University Malaya Medical Centre (UMMC), Kuala Lumpur were carried out as per institutional protocol. Routine computed tomogram (CT) angiography for donor evaluation showed incidental finding of urolithiasis. All donors with urolithiasis were extensively evaluated, and risk stratified on their lithogenic future risks. Various investigations, including complete metabolic profiling were conducted to ensure the well-being of the remaining kidney. Donors with a history of symptomatic urolithiasis, bilateral nephrolithiasis, or incidental stone larger than 1 cm were excluded from kidney donation consideration. Additionally, donors were subjected to a 24-hour urinalysis to screen for metabolic risk factors for renal stones which included hypercalciuria, hypocitraturia, hyperuricosuria, and hyperoxaluria. In addition, these donors were also screened for conditions such as gout, hyperparathyroidism, and hypophosphatemia. After a multidisciplinary team (MDT) discussion, donors with incidental renal stones that fulfil the donor expanded criteria proceeded to ex-vivo bench surgery.

Intra-operative Steps

Donor nephrectomies were done laparoscopically through the transperitoneal route. The donor-kidney was placed in ice-slush once harvested and perfused with preservation solution as per our institutional protocol. Flexible uretero-renoscope (URS) was then introduced without dilatation of the ureteral stump under low-flow continuous irrigation with direct vision. Ice-cold physiologic saline irrigation was used throughout the procedure to ensure cold ischemia while keeping the graft and ureter submersed under preservation fluid. All adjuncts for stone management such as stone basket and Holmium laser were available if needed. Following the completion of the procedure, the donor kidney was transferred to the recipient for implantation.

Follow-Up Protocol

All donors and recipients were followed up by the nephrologist as per institutional protocol with blood works and an ultrasound of the kidneys at 6 months and 1 year. Surveillance was aimed to detect any new stones.

Demographic data included both donor and recipients including age, sex, location and number of stones, stone size, endourology technique, operative time, intraoperative and postoperative complications, stone-free status, stone recurrence in both donor and recipient, and renal allograft function were recorded.

Result

Between 2019 to 2022, a total of four donors in UMMC had incidental non-obstructing renal stones during pre-transplant evaluation on preoperative CT scan. There were no alternative donors for these recipients therefore an expanded criteria were adhered to permitting these transplants. The demographic data of the donors in this series is shown in Table 1. The mean age of the donors were 42 years old (range 36-45). Stones were between 3-4mm at mainly the lower pole of the kidney based on the CT images preoperatively.

Table 2 shows the summary of intra-operative procedures and outcomes in our study. All collecting system of the graft kidney were visualised using flexible URS. Only one case encountered a stone that was successfully removed using a stone basket. In the remaining three grafts, no stone were found, and radio-opacity seen in the preoperative CT turned out to be Randall's plaques, a common benign finding, that pose little to no risk of future obstruction. The additional operative time required for ex-vivo stone management ranged from 16-25 minutes. No immediate complications were encountered during the ex-vivo bench surgery and there was no compromise in the early graft function or cases of graft rejection after 1 year of follow up. Both the donors and the recipients were well, and no new occurrences of urolithiasis.

Table 1: Patient Demographics

Patient	Age/ Sex	Number of stone	Stone size (mm)	Stone Location (Pole)
1	36/F	1	3	Lower
2	45/F	1	3	Middle
3	45/F	1	4	Lower(duplex system)
4	42/M	1	3	Lower

Table 2: Summary of Intra-operative Procedures and Outcomes

Patient	Procedure	Stone Status	Additional Ex-Vivo Time (mins)	Intraop/Postop Complication	Graft Function	Stone Recurrence (Donor/Recipient)
1	Flexible URS	Randall's plague	25	No	Good	No
2	Flexible URS	Randall's plague	18	No	Good	No
3	Flexible URS	Cleared	16	No	Good	No
4	Flexible URS	Randall's plague	24	No	Good	No

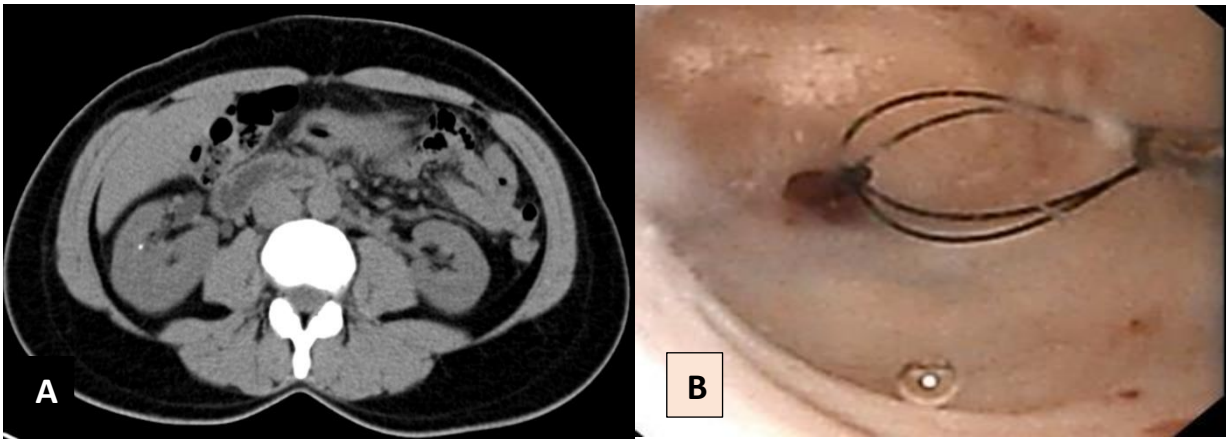

Figure 1: A: Preoperative CT showing a small non-obstructing right renal calculus. **B:** Intraoperative image of ex-vivo flexible uretero-renoscopy and basketing done to retrieve the renal calculus.

Discussions:

The demand for solid organs has outweighed the availability of viable organ at the opportune moment. Various factors have led up to this moment crossing paths with cultural, psychological barriers to donation and missed opportunities to consent for donation. We have come a long way from shifting our views on patients with asymptomatic urolithiasis as non-ideal donors. Historically, conventional imaging with ultra-sonography (USG) and intra-venous urography (IVU) for donor assessment would have missed these asymptomatic renal calculi, and patient will proceed with renal transplantation. However, with the advent of CT imaging, these potential donors were deemed ineligible[6].

Concerns were met with guidelines. In 1996, the Ad Hoc Clinical Practice Guidelines Subcommittee of the Patient Care and Education Committee of the American Society of Transplant Physicians stated that "nephrolithiasis is at least a relative contraindication to living donor nephrectomy because of the future risk that recurrent stones, obstructions, and infections will injure the remaining kidney" and that "nephrolithiasis not only places the donor at risk; inadvertent transplantation of a kidney with stone places the recipient at risk"[7] . However, the outlook of renal transplant took a turn when the transplant surgeons discussed thoroughly regarding this in International Forum on the Care of the Live Kidney Donor in 2004. The forum outlined the possibility an asymptomatic potential donor with a current single stone might be considered suitable for kidney donation if (a) there is no hypercalciuria, hyperuricemia, or metabolic acidosis; (b) there is no cystinuria or hyperoxaluria; and (c) the stone measures <15 mm in size or potentially removable during transplant[9]. When evaluating a potential kidney donor with an incidental asymptomatic renal stone options include the donation of the non-stone bearing kidney, donation of the stone-bearing kidney without stone removal, stone removal prior to planned transplant, and ex-vivo stone removal at the time of transplant[10].

In our series, one out of the four patients who had asymptomatic renal stone from preoperative imaging had the stone removed ex-vivo prior to implantation while the remaining three patients, stone was not encountered during the bench-surgery and proceeded with implantation. With proper case selection, the current endourological armamentarium, have made it possible to obtain stone clearance in the graft kidney at the time of living-donor nephrectomy through ex-vivo surgery. However, no clear guidelines exist about the optimal operative management of graft urolithiasis. We used a combination of flexible uretero-renoscopy (URS) scopes and stone baskets. The flexi-URS scope was used without an access sheath with continuous low cold irrigation fluid. On the contrary to flexible scopes, semi-rigid URS has been reported to be equally efficacious in the stone management of graft kidney [11]. With the graft detached, manipulation of the ureter to align the desired calix with the axis of the ureteroscope allows access to the collecting system with minimal risk of trauma to the ureter[12].

Larger stones may require additional fragmentation to facilitate complete clearance which could be safely done with the Holmium laser. Some authors consider this as a better option than conventional pneumatic lithotripters as the explanted graft lacks firm support which could add to a potential mucosal injury[13].

Transplant surgeries in general including renal transplant, are working against the clock to minimise the ischemic time. It has been shown that cold ischemia time of the kidney >8 hours have been shown to impair renal function, increasing rejection rates, while affecting long-term graft survival[14]. In our series, ex-vivo procedure adds minimal cold ischemia time, with mean time of approximately 20 minutes. The detached graft ureter and kidney allows greater degree of manipulation needed to align the axis of the scope with the calix. This freedom of movement allows quick access to the collecting system while being cautious not to injure the ureter.

None of the recipients who received graft from living donors who underwent ex-vivo procedure had any early postoperative complications related such as ureteric injury, haematuria, urine leak, or early graft dysfunction. Several risk-reduction strategies have been proposed to prevent ureteral injury during ex-vivo endourologic manipulations which includes minimal handling of the ureter, a minimum influx of irrigation fluid to prevent the potential for pyelovenous and pyelolymphatic backflow, usage of smaller instruments, and placement of a double-J ureteral stent during the neo ureteroneocystostomy anastomosis[15].

In our experience, endoscopic extraction of renal stone in the donor kidney at the time of transplantation was done in one patient. In remaining three patients, the previously identified stone from the preoperative scans were not encountered, instead we found Randall's plague, posing little to no risk of future obstruction. Kidneys were successfully transplanted with no new recipient recurrences while the in-situ stones in the graft were stable at more than 1 year of follow-up.

Regarding the impact of graft function, cases from our centre suggests that graft function is not compromised. No immediate complications or graft dysfunction were reported following implantation of grafts with ex-vivo stone clearance. However, it is important to consider that long term follow-up and larger studies are needed to fully evaluate the impact of this technique on graft function and outcomes.

Ex-vivo stone clearance aims to prevent potential complications associated with stone-related issues in the transplanted kidney, such as infection, obstruction, or recurrent stone formation. By removing the stone before implantation, risk to both the donor and recipient is minimized. Ex-vivo clearance of renal stones during renal transplant has been used successfully in some cases including cases from our centre. It is important to note that it is still a relatively controversial procedure.

Ultimately, decision to perform ex-vivo stone clearance should be made on a case-by-case basis. Multidisciplinary team (MDT) discussion, involving the transplant surgeon, nephrologist, urologist, anaesthetist, and other relevant specialists. Individualized assessment of the specific case, considering the risks and benefits, will help to determine whether ex-vivo clearance is appropriate. considering factors such as the size and characteristics of the stone, the overall health of the donor and recipient and most importantly the experience and expertise of the transplant team. Preoperative evaluation and careful selection of donors with asymptomatic renal stones are crucial to ensure safety and success of the procedure.

Conclusions:

Ex-vivo clearance of renal stones during transplant represents a potential solution to manage asymptomatic renal stones in selected donors, with the goal of increasing the available pool of organs

for transplantation. Ongoing research and continued long-term follow-up of donors and recipients are essential to refine the technique and establish the optimal operative management.

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