

Peer Review File

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Reviewer A

1, Left kidney stone is not staghorn stones. You should change the expression.

Reply 1: Thank you for pointing this out, we agree and have changed it to left renal stone throughout the manuscript and the title.

Changes in the text:

“Left endoscopic combined intrarenal surgery with electrocoagulation hemostasis and right flexible ureteroscopic lithotripsy for bilateral upper urinary tract stones: a case report” Title, Page 1, lines 2 – 4.

“We report the case of a 36-year-old male with a large left renal pelvis stone, right proximal ureteric stone, and bilateral renal stones.” Abstract, Page 2, lines 44 – 45.

“The hybrid operation in split-leg prone position was successfully performed on a 36-year-old hypertensive male with left renal pelvis stone, right upper ureteric stone, and bilateral renal stones.” Page 3, lines 86 – 89.

“Preoperative CT revealed a left renal pelvis stone (max diameter 25.9 × 16.0 mm; max density 1898 Hounsfield Units [HU]; Guy’s stone score [GSS] Grade II), right proximal ureteric stones (max diameter 10 × 5 mm; max density 1918 HU), bilateral renal stones, and mild hydronephrosis, and left adrenal gland hyperplasia (Figure 1).” Page 3, lines 100 – 103.

“A rigid 8/12 Fr ureteroscope (Richard Wolf, Germany) was inserted via the guidewire to access the pelvis and the left renal stone was identified.” Page 4, lines 132 – 133.

2, CT finding showed bilateral hydronephrosis. Therefore, renal function might be worried. You have to add the kidney function like Cre, eGFR etc.

Reply 2: Thank you for pointing this out. The patient’s serum creatine levels were normal pre- and post-operatively. We have added it into the biochemical results.

Changes in the text:

“Biochemical results revealed elevated white blood cell count ($13.97 \times 10^9/L$), C-reactive protein (11.21 mg/L), HbA1C (6.2%), and normal creatine (93 $\mu\text{mol/L}$).” Page 3, lines 95 – 97.

3, Maybe, renal function is decreasing. So, did you consider the pre-stenting for bilateral side or one side??

Reply 3: Thank you for your question. Upon admission, the patient’s renal functions were normal. We have included the creatine level in the manuscript. The patient opted for a single-session stone retrieval than undergoing pre-stenting prior elective flexible ureteroscopy. Therefore, it was considered but we respected the patient’s choices. It was stated in the manuscript as “Our team of specialists discussed the management plan with the patient, to which he consented to undergo an elective hybrid procedure to decrease the risk of postoperative complications and duration of hospital stay.”

Changes in the text:

“Biochemical results revealed elevated white blood cell count ($13.97 \times 10^9/L$), C-reactive protein (11.21 mg/L), HbA1C (6.2%), and normal creatine (93 $\mu\text{mol/L}$.)” Page 3, lines 95 – 97.
“Our team of specialists discussed the management plan with the patient, to which he consented to undergo an elective hybrid procedure to decrease the risk of postoperative complications and duration of hospital stay. He refused pre-stenting and elective surgery despite raised inflammatory markers.” Page 3, lines 104 – 108.

4, What size of rigid nephroscope did you use? You broke the stones using LithoClast master. What type of probe did you use because your tract size seems to be 18Fr?, so probe size and nephroscope size were restricted.

Reply 4: Thank you for your question. We apologize for some mistakes. The rigid nephroscope we used was from Richard Wolf, IL, USA. The probe we used was the Swiss LithoClast™ Select pneumatic lithotripsy probe (2.0 mm \times 425 mm). We have made the respective changes.

Changes in the text:

“A rigid 8/12 Fr ureteroscope (Richard Wolf, Germany) was inserted via the guidewire to access the pelvis and the left renal stone was identified. Pneumatic lithotripsy (Swiss LithoClast® Select, Boston Scientific, NJ, USA) was performed with a 2.0 mm \times 425 mm probe.” Page 4, lines 132 – 135.

5, You coagulated the bleeding point with electronic instrument. Please show some photos as pictures. It is a very helpful for readers to understand.

Reply 5: Thank you for your interest. Unfortunately, we did not have preoperative images of the coagulation process. Instead, a picture of the electrocoagulation device with its three probes.

Changes in the text:

“Our institute patented a microchannel hemostatic device that has different detachable electrodes (Figure 2).” Page 4, lines 140 – 141.

“The electrocoagulation device used intraoperatively with its three different detachable electrodes (1 to 3) that can be attached to the rigid nephroscope. The probe tips have different diameters and angles to facilitate hemostatic electrocoagulation.” Legends, Figure 2, page 10, lines 344 – 346.

Reviewer B

First of all, congratulations for achievement this surgery.

Although the topic name is ECIRS(Endoscopic Combined Intrarenal Surgery) but the procedure that you describe in manuscript looks as only be PCNL.

To make your MS better, i humbly suggest some comment to you.

1. Share the benefit of combine double scope (PCNL and URS) ex. pass the ball technique with stone relocation, endovision guidance puncture. That make ECIRS MS look more interesting.

Reply 1: Thank you for your suggestions. We have rewritten the surgical procedure in detail and added the benefits of this technique in DISCUSSION.

Changes in the text:

“The combination of double scope contributed greatly to procedural success.” Page 6, line 214.

“Because FURS is performed through the natural orifice in antero- and retrograde approach and can be inserted via the PCNL channel, the risk of severe bleeding due to injury of renal parenchyma has also been significantly diminished by reducing the number of tracts [18]. This endovision-guided puncture was found feasible in prone position [19]. In addition, stones can be displaced in a more convenient location for the nephroscope, also known as “pass-the-ball” technique [20]. The aforementioned techniques greatly benefits final clearance status.” Page 6, lines 216 – 222.

References:

Serra S, Corona A, Caddeo G, De Lisa A. L'approccio Endovision nella litotriassia percutanea endorenale [The Endovision technique in renal percutaneous lithotripsy]. *Urologia*. 2012;79 Suppl 19:125-127. Published 2012 Dec 30. doi:10.5301/RU.2012.9521

Undre S, Olsen S, Mustafa N, Patel A. "Pass the ball!" Simultaneous flexible nephroscopy and retrograde intrarenal surgery for large residual upper-pole staghorn stone. *J Endourol*. 2004;18(9):844-847. doi:10.1089/end.2004.18.844

2. Write more clear in term of PCNL system(size of PCNL sheath , Nephroscope size and manufacture name....) I guess that you applied rigid URS to be rigid nephroscope? It's very important information tho know what type of equipment that you use?

Reply 2: Thank you for your questions. We have added the equipment details as below.

Changes in the text:

“A rigid 8/9.8 Fr ureteroscope (Richard Wolf GmbH, Knittlingen, Germany) was directly inserted and revealed a normal bladder.” Page 3, lines 109 – 111.

“The proximal ureteric stone was identified and pulverized by holmium laser lithotripsy (VersaPulse® PowerSuite™ 100W, LUMENIS, CA, USA) at 1.0 W, 15 Hz setting.” Page 3, lines 112 – 113 and page 4 line 117.

“A rigid 8/12 Fr ureteroscope (Richard Wolf, Germany) was inserted via the guidewire to access the pelvis and the left renal stone was identified. Pneumatic lithotripsy (Swiss LithoClast® Select, Boston Scientific, NJ, USA) was performed with a 2.0 mm × 425 mm probe.” Page 4, lines 100 – 103.

3. I do not understand meaning of "Combined ECIR and tubeless micro PCNL" in Key finding and "ECIR" in conclusion. ECIR stand for? (or you plan to use ECIRS term?)

Reply 3: Thank you for your question. We apologize for the mistake, the correct abbreviation is ECIRS, which we clarified to be performed in the left upper urinary tract, because it consisted of mini PCNL, hemostatic electrocoagulation to achieve tubeless PCNL, and retrograde flexible ureteroscopy.

Changes in the text:

“Under split-leg prone position, we performed a hybrid procedure that left tubeless single-tract mini PCNL, left flexible ureteroscopy, and right flexible ureteroscopic lithotripsy.”
Abstract, Page 2, lines 45 – 47.

“Endoscopic combined intrarenal surgery (ECIRS) combines PCNL with retrograde intrarenal surgery (RIRS) in a minimally invasive method.” Page 2, lines 79 – 80.

“In this study, we report our initial experience with a single-session bilateral endoscopic surgery – left ECIRS with tubeless PCNL where hemostasis was achieved by transcatheter electrocoagulation, left flexible ureteroscopy, and right flexible ureteroscopic lithotripsy.”
Page 3, lines 84 – 86.

4. Blood chem shows white blood cell count ($13.97 \times 10^9 /L$), C-reactive protein (11.21 mg/L), and HbA1C (6.2%). It still be infection in KUB system? MicroPCNL is a high intrarenal pressure procedure, it is better if we treat infection first. If already treat what is the result? Negative urine culture?

Reply 4: Thank you for your question. We agree that urinary tract infections should be controlled first. Despite the elevation in inflammatory markers, the patient did not have fever or obvious signs of infection. Urine culture was negative. The patient was given the choice to undergo pre-stenting before elective surgery or 3-day prophylactic antibiotic therapy before undergoing a single-session operation. He chose the latter.

Changes in the text:

“Antihypertensives and a 3-day prophylactic antibiotic therapy with Augmentin was initiated upon admission. Our team of specialists discussed the management plan with the patient, to which he consented to undergo an elective hybrid procedure to decrease the risk of postoperative complications and duration of hospital stay. He refused pre-stenting and elective surgery despite raised inflammatory markers.” Page 3, lines 103 – 108.

I hope you will success for submission in next version.

Reviewer C

Thank you for this interesting case report. I have some questions that I hope you can clarify with a subsequent revision of the manuscript.

1) In Line 49 you have correctly defined what ECIRS is - retrograde intrarenal surgery and PCNL in the same renal unit. From Line 75 onwards, you seem to have described right retrograde intrarenal surgery followed by left PCNL - this is not what the standard definition of ECIRS is.

Reply 1: Thank you for pointing this out. We apologize for not detailing the surgery properly. The patient received ECIRS for the left renal stone. We have rewritten the case description.

Changes in the text:

“Under split-leg prone position, we performed a hybrid procedure that left tubeless single-tract mini PCNL, left flexible ureteroscopy, and right flexible ureteroscopic lithotripsy.” Abstract, Page 2, lines 45 – 47.

“Endoscopic combined intrarenal surgery (ECIRS) combines PCNL with retrograde intrarenal surgery (RIRS) in a minimally invasive method.” Page 3, lines 79 – 80.

“In this study, we report our initial experience with a single-session bilateral endoscopic surgery – left ECIRS with tubeless PCNL where hemostasis was achieved by transcatheter electrocoagulation, left flexible ureteroscopy, and right flexible ureteroscopic lithotripsy.” Page 3, lines 84 – 86.

“To check for residual stones, a disposable digital FURS (RedPine, Guangzhou, China) was inserted via the PCNL tract and another flexible ureteroscope was accessed via the lower urinary tract.” Page 4, lines 135 – 137.

2) In Line 83 and 84, you have stated that you inserted a 5F double-J stent followed by a 6Fr ureteroscope catheter into the right ureter. Can you clarify if you meant a ureteric catheter, as well as the reason for having both a ureteric stent and a ureteric catheter on the right side after having completed fURS on this side?

Reply 2: Thank you for your question. Bilateral operations were performed simultaneously. We first described the right procedure as we required bilateral flexible ureteroscopy and D-J stenting towards the end of the procedure. We apologize for using the term ‘ureteric catheter’ when the correct term is ‘ureteral catheter’, which is used to induce artificial hydroureteronephrosis to facilitate mini PCNL in the left.

Changes in the text:

“A 25 cm 6 Fr ureteral catheter was introduced into the left ureter. This was done to induce artificial hydroureteronephrosis to facilitate mini PCNL in the left.” Page 4, lines 121 – 123.

3) Line 88 stated that the PCNL needle used was 18Fr - I assume that you meant an 18G needle?

Reply 3: Thank you for pointing this out. We indeed meant an 18 G needle. It has been corrected.

Changes in the text:

“An 18 G PCNL needle was inserted against the lateral aspect of the probe after estimating a suitable angle.” Page 4, lines 126 – 127.

4) In Line 92 it is mentioned that the tract was dilated from 8 to 18Fr using sequential dilators. Could you clarify what was the sheath size used (if any) for the PCNL procedure? 18Fr would classify the nature of the PCNL as a mini PCNL rather than a micro PCNL. (Desai et al. Curr Opin Urol 2012)

Reply: Thank you for your question and suggestions. Indeed, we used an 18 Fr sheath. We have read the article by Desai et al. and we agree that we made a mistake writing it as micro-PCNL. We have changed it to mini-PCNL throughout the manuscript and title.

Changes in the text:

“This was done to induce artificial hydroureteronephrosis to facilitate mini PCNL in the left.” Page 3, lines 122 – 123.

“In our patient, we have successfully combined several developing techniques within a single session, this hybrid procedure consisted of split-leg prone position, extraplanar USG for PCNL needle access, simultaneous anterograde-retrograde FURS approach with lithotripsy, and tubeless single-tract mini PCNL with transcatheter electrocoagulation hemostasis.” Page 5, lines 163 – 167.

“Unilateral ECIRS with tubeless single-tract mini PCNL with electrocoagulation hemostasis and adjacent retrograde intrarenal surgery in split-leg prone position is a safe, feasible, and efficient technique to manage large renal stones.” Page 6, lines 230 – 232.

5) During the PCNL procedure, was retrograde access performed on the same side (left side) at all? If not then the nature of the procedure performed is a PCNL and not ECIRS.

Reply: Thank you for your question. Retrograde access was also performed in the left side, we apologize for not writing it clearly.

Changes in the text:

“Under split-leg prone position, we performed a hybrid procedure that left tubeless single-tract mini PCNL, left flexible ureteroscopy, and right flexible ureteroscopic lithotripsy.” Abstract, Page 2, lines 45 – 47.

“In this study, we report our initial experience with a single-session bilateral endoscopic surgery – left ECIRS with tubeless PCNL where hemostasis was achieved by transcatheter electrocoagulation, left flexible ureteroscopy, and right flexible ureteroscopic lithotripsy.” Page 3, lines 84 – 86.

“To check for residual stones, a disposable digital FURS (RedPine, Guangzhou, China) was inserted via the PCNL tract and another flexible ureteroscope was accessed via the lower urinary tract.” Page 4, lines 135 – 137.

6) The CT scan images performed suggest that the stone on the left side was a large renal pelvis calculus rather than a staghorn calculus, both based on image as well as the size measurements. Could you clarify on the exact type of stone that was treated? Using a validated stone scoring system may also help (eg Guy Stone Score).

Reply: Thank you for your question. We apologize to writing it a staghorn calculus. We have changed it to large left renal calculus throughout the manuscript. According to the Guy’s Stone Score, the type of stone treated belongs to Grade II.

Changes in the text:

“Left endoscopic combined intrarenal surgery with electrocoagulation hemostasis and right

flexible ureteroscopic lithotripsy for bilateral upper urinary tract stones: a case report” Title, Page 1, lines 2 – 4.

“We report the case of a 36-year-old male with a large left renal pelvis stone, right proximal ureteric stone, and bilateral renal stones.” Abstract, Page 2, lines 44 – 45.

“The hybrid operation in split-leg prone position was successfully performed on a 36-year-old hypertensive male with left renal pelvis stone, right upper ureteric stone, and bilateral renal stones.” Page 3, lines 86 – 89.

“Preoperative CT revealed a left renal pelvis stone (max diameter 25.9 × 16.0 mm; max density 1898 Hounsfield Units [HU]; Guy’s stone score [GSS] Grade II), right proximal ureteric stones (max diameter 10 × 5 mm; max density 1918 HU), bilateral renal stones, and mild hydronephrosis, and left adrenal gland hyperplasia (Figure 1).” Page 3, lines 100 – 103.

“A rigid 8/12 Fr ureteroscope (Richard Wolf, Germany) was inserted via the guidewire to access the pelvis and the left renal stone was identified.” Page 4, lines 132 – 133.

7) Would you be able to provide images of the transcatheter haemostatic device, and comment on whether it has been previously used in PCNL cases for a similar indication? Or is this the first known use of this device in PCNL for this indication?

Reply: Thank you for your interest and question. Yes, we have included a Figure 2 that shows the electrocoagulation device with its 3 electrodes. Tubeless PCNL by electrocauterization was described in previous literature (Joe et al.) who also designed their own device. The electrocoagulation device used in study was an original design and patented item register in China. Currently, it is still in a clinical trial. Therefore, we may not be the first to apply such concept, but this is the first utilization of such a device with detachable electrode head that can be connected to the rigid ureteroscope.

Changes in the text:

“Our institute patented a microchannel hemostatic device that has different detachable electrodes (Figure 2).” Page 4, lines 140 – 141.

“The electrocoagulation device used intraoperatively with its three different detachable electrodes (1 to 3) that can be attached to the rigid nephroscope. The probe tips have different diameters and angles to facilitate hemostatic electrocoagulation.” Legends, Figure 2, page 10, lines 344 – 346.

References:

Jou YC, Cheng MC, Sheen JH, Lin CT, Chen PC. Electrocauterization of bleeding points for percutaneous nephrolithotomy. *Urology*. 2004;64(3):443-447.
doi:10.1016/j.urology.2004.04.078

8) Could you clarify if the fURS on the right side, was performed simultaneously with the PCNL on the left side? If so then this actually describes the technique of Simultaneous Bilateral Endoscopic Surgery (SBES) as described by Giusti et al. (Eur Urol 2018 Dec) although the original description was for surgery in the supine rather than prone position.

Reply: Thank you for stating this out. Yes, both procedures were performed simultaneously. We appreciate the article you have shared to add insight to the study.

Changes in the text:

“Simultaneously, a single PCNL tract was established under extraplanar ultrasonography (USG)

guidance: The C251 Curved Array transducer and ALOKA ARIETTA60 (Hitachi Medical Corp., JPN) were used.” Page 4, lines 124 – 126.

“In our patient, we have successfully combined several developing techniques within a single session, this hybrid procedure consisted of split-leg prone position, extraplanar USG for PCNL needle access, simultaneous anterograde-retrograde FURS approach with lithotripsy, and tubeless single-tract mini PCNL with transcatheter electrocoagulation hemostasis.” Page 4, lines 163 – 167

9) The patient was discharged only on the 4th post operative day although the Foley catheter was removed on the 1st post operative day. Could you explain why the patient stayed for 4 days given the minimally invasive, tubeless nature of the procedure?

Reply: Thank you for your question. As this device is still under clinical trial, we were not certain about the postoperative recovery and therefore asked the patient to remain hospitalized for observation before being discharged. Overall, the duration of hospital stay is still lower and the patient was satisfied.

Changes in the text:

“The Foley catheter was removed on day 1 post-operation and he was discharged on the fourth once we confirmed that there was no bleeding complication.” Page 4, lines 148 – 150.

10) What was the indication to use electrocoagulation in this case, and what is your standard practice?

Reply: Thank you for your question. Hemorrhage is a common complication for patients that have undergone PCNL. The main reason that electrocoagulation was performed was because the patient did not have any obvious remaining stones and the head surgeon deemed it unnecessary to receive a secondary procedure. Therefore, to decrease the need for a PCNL tube, electrocoagulation was performed. Our standard practice is pre-stenting before elective retrograde intrarenal surgery. However, the patient refused.

Changes in the text:

“Our team of specialists discussed the management plan with the patient, to which he consented to undergo an elective hybrid procedure to decrease the risk of postoperative complications and duration of hospital stay. He refused pre-stenting and elective surgery despite raised inflammatory markers.” Page 3, lines 104 – 108.

Reviewer D

The manuscript is interesting. Simultaneous surgery is worthwhile pursuit. I read with interest about the nuances of the author's approach including the use of a novel device.

Compositional review and proofreading required throughout. For example "procedures may be necessitated to achieve stone clearance." Also, abbreviations should be defined the first time they appear in the text (e.g. ECIR).

Reply 1: Thank you for your comment. We apologize for using ECIR when it should be ECIRS.

Changes in the text:

"Endoscopic combined intrarenal surgery (ECIRS) combines PCNL with retrograde intrarenal surgery (RIRS) in a minimally invasive method." Page 3, lines 79 – 80.

"However, multi-tract or staged procedures may be necessitated in bilateral or anatomically-complex stones to achieve stone clearance." Abstract, Page 2, lines 40 – 41.

What laser settings we used for fragmentation.

Reply 2: Thank you for your question. The energy setting of the holmium laser was 1.0 W, 15 Hz.

Changes in the text:

The proximal ureteric stone was identified and pulverized by holmium laser lithotripsy (VersaPulse® PowerSuite™ 100W, LUMENIS, CA, USA) at 1.0 W, 15 Hz setting." Page 3, lines 112 – 113 and page 4 line 117.

What does "beneath the ureteric stones" mean? What is a flexible ureteroscope catheter?

Reply 3: Thank you for the question. We apologize for the poor wording. A disposable FURS was accessed through the PCNL channel and another retrograde FURS was inserted via the lower urinary tract. Therefore, the retrograde access reaches beneath the ureteric stone. A peel-away sheath was used and not a FURS catheter.

Changes in the text:

"To check for residual stones, a disposable digital FURS (RedPine, Guangzhou, China) was inserted via the PCNL tract and another flexible ureteroscope was accessed via the lower urinary tract." Page 4, lines 135 – 137.

How was 2 mm stone cutoff decided for leaving fragments in situ.

Reply 4: According to literature, stones < 5 mm are considered insignificant residual stones. The European Association of Urology deem these stones less likely to require intervention. Two millimeters was our cutoff point because these stones were difficult to extract. In this operation, we used the COOK NGage Nitinol Stone Extractor.

Changes in the text: None.

Was the electrocautery probe introduced through the ureteroscope of under imaging guidance through the sheath itself? Can you describe this technique further? Is it pulled back simultaneously with the sheath?

Reply 5: Thank you for your question. The diameter of the electrocautery probe was larger than

the rigid ureteroscope. Therefore, the body of the electrode had to be inserted from the tip of the rigid ureteroscope to be attached and not introduced via the ureteroscope.

Changes in the text:

“Bleeding points were inspected through the rigid 8/12 Fr ureteroscope. Our institute patented a microchannel hemostatic device that has different detachable electrodes (Figure 2). As the electrode probe tip’s diameter was larger than the rigid ureteroscope channel (6 Fr), it had to be inserted via the proximal opening of the rigid ureteroscope before connecting to the power source. Hemostasis was achieved by introducing the combined device through the PCNL channel and performing electrocauterization.” Page 4, lines 108 – 113.

Was retrograde ureteroscope also performed on the left? There is discussion about simultaneous retrograde and antegrade approach ipsilaterally throughout the manuscript.

Reply 6: Thank you for your question. Bilateral retrograde ureteroscope was performed: the right side to perform lithotripsy and the left to find residual stones.

Changes in the text:

“To check for residual stones, a disposable digital FURS (RedPine, Guangzhou, China) was inserted via the PCNL tract and another flexible ureteroscope was accessed via the lower urinary tract.” Page 4, lines 135 – 137.

Based on figure 2, it appears that bilateral stents were placed, but this is not discussed in the technique.

Reply 7: Thank you for pointing this out. Because this procedure included a left-side tubeless PCNL and that the device is still under clinical trial, the surgeons thought it better to perform bilateral D-J stenting as a safety precaution. We have added this explanation into discussion.

Changes in the text:

“After confirming no residual stone, a 5 Fr ultra D-J stent was retained as a precaution for tubeless PCNL. The ureteroscope was withdrawn and a 16 Fr Foley catheter was retained.” Page 4, lines 137 – 139.

A figure showing the electrocautery probe and technique would be helpful.

Reply 8: Thank you for your interest. We have included an image of the device as a new Figure 2. Unfortunately, we currently do not have a figure regarding intraoperative technique.

Changes in the text:

“Our institute patented a microchannel hemostatic device that has different detachable electrodes (Figure 2).” Page 4, lines 140 – 141.

“The electrocoagulation device used intraoperatively with its three different detachable electrodes (1 to 3) that can be attached to the rigid nephroscope. The probe tips have different diameters and angles to facilitate hemostatic electrocoagulation.” Legends, Figure 2, page 10, lines 344 – 349.