

Peer Review File

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Reviewer A

The purpose of this study was to evaluate whether stone extraction with a loop ureteral catheter (LUC) is associated with a higher frequency of ureteral strictures in distal ureteral stones compared to treatment with primary ureteroscopic stone removal (p-URS) or ureteroscopic laser lithotripsy (I-URS). The authors extracted data from 547 patients at a single institution between 2005 and 2019. They report no difference in ureteric strictures, which were also very uncommon, concluding that LUC stone extraction is an effective endourological procedure and alternative to ureteroscopic procedure in stone management.

Comment 1: In the abstract, the authors state that “ureteric strictures were very uncommon in all procedures and there was no difference between the groups” – it would be useful to also report the number or proportion rather than the p-value alone.

Reply 1: We appreciate this important notice and added the numbers of ureteric strictures to the abstract and in the main text.

Changes in the text: Please find the changes on page 2, lines 21-23 in the “results” section of the abstract and on page 12, lines 14-15 in the “Discussion/Conclusions” section of the main text.

Comment 2: In the Introduction, the authors state that the LUC literature for stone extraction is rare, but why might this be the case? Additional context is needed here. For example, is this a new(er) procedure? Has it just been adopted in this country or region compared to elsewhere? The phrasing “rare” does imply some literature – what has this reported (anything in addition to reference 8)? And why is this the procedure of choice in this department/institution (perhaps compared to other institutions)?

Reply 2: We thank the reviewer for stating this important issue. Loop guided stone extraction was implemented in the 1930s in Germany. During that time, publication of clinical data or performance of comparative studies was not as common as these days, which, at least in part, explains the low number of literature. Additionally, the emergence of endoscopic instruments and the beginning of visualized stone removal fundamentally changed the means of treatment. Ureteroscopy, of course, is the procedure of choice in most of the cases in our department. But in some cases, loop guided stone extraction still is an option, illustrating diversity of modern stone treatment.

Changes in the text: We complemented the “Introduction” section (page 4, lines 17-26) and the “Discussion/Conclusions” section (page 12, lines 15-19) and supplemented some literature (Ipiens-Aznar et al., Darwish et al., de la Rosette et al., Fam et al.).

Comment 3: On this note, if this procedure is relatively under-described, why was ureteral stricture specifically chosen as the outcome variable?

Reply 3: At the time before endoscopic visualized stone removal, loop guided procedures were the only alternative for lithotomy. The loop guided techniques were used for all locations of ureteric stones (distal stones as well as proximal stones). As even more severe complications like ureter rupture do not occur in well selected patients, we chose ureteric stricture as the worst expected outcome variable.

Changes in the text: See changes in the text as stated in comment 2.

Comment 4: It might be useful for the authors to comment on why LUC or URS was performed, as they state in their Techniques simply that one or the other was performed. If they are describing that this procedure is as appropriate as others, how this decision was made (since they later describe no difference in demographic variables of patients) might be useful for practitioners.

Reply 4: We are grateful for this advice and complemented a statement in the main text.

Changes in the text: You can find the complemented statement on page 11, lines 25 to page 12, line 2 in the “Discussion/Conclusions” section of the main text.

Comment 5: The authors report there was no difference between the groups for demographic characteristics such as age, gender, patients with stenting – how about differences by surgeon, location (if applicable), size of stone, contact by mail vs. telephone, or when this procedure was performed (i.e. to account for “practice effects” after initial adoption)?

Reply 5: We included stone size in Table 1. In LUC, stone size was smaller compared to the other groups (4.0mm in the LUC vs. 4.4mm in the p-URS and 4.8mm in the l-URS group).

The location of the ureteral stone was the very distal part of the ureter in all cases. The entrance of the ureter into the small pelvis, visualized by crossing the iliopectineal line has proven to be the most reliable definition of the distal ureter. In detail, the present study refers to ureteric stones that also passed the crossover of the common iliac arteries.

All patients were contacted either by phone or mail, we did not differentiate between these modalities. When patients could not be contacted, we applied to their general practitioner or office-based urologist. Main reason for unanswered questionnaires was moving of the patients to a new address or lack of interest in taking part in our survey. We then evaluated based on the medical reports.

The handling of loop guided stone extraction belongs to the interventional portfolio in our department and was not abolished during the implementation of endoscopic visualized procedures. All surgeons had at least seven years of surgical experience.

To generate a greater differentiation in our set of data, we augmented Table 1 and Table 2 and evaluated differences in hospitalization, readmission <3 months and operating time.

Changes in the text: We augmented Tables 1 and 2 (see there and changes in the main text on page 17, lines 10-16) and complemented the “Methods” section (page 7, lines 15-17) and the “Results” section (page 8, lines 23-25 and page 9, lines 8-9). We also complemented the “Results” section in the abstract (page 2, lines 20-21).

Comment 6: The authors report that 412 patients treated by URS (p-URS n=304, I-URS n=108) and another 135 by LUC stone extraction. How do these proportions compare to either other institutions or other published data? This information would be useful for generalization outside of this single institution.

Reply 6: As the loop guided procedures were nearly abandoned after implementing endoscopic visualized techniques, we only can refer to one study from 1983. Lynn et al. describe interventional therapies in 99 patients, 58 of which were treated by loop guided technique and another 7 by basket stone extraction. Unfortunately we have no knowledge about the use of loop guided procedures in other institutions at present and are looking forward to the feedback from the urology community after publishing this uncommon set of data.

Changes in the text: We did not perform changes in the text concerning this comment.

Comment 7: Similarly, the authors report that ureteric stricture was rare (3 + 2 + 2), how does this rate compare to the literature or other institutions?

Reply 7: Perez Castro et al. included 9681 patients with ureteric urolithiasis in a large multi-institutional study recruiting patients from 32 countries. In 4479 cases a distal ureteric stone was diagnosed and treated by ureteroscopy. 83 of these patients (1,9%) had ureter obstruction/stricture or needed to be retreated within 3 months. This is in line with the present results in our cohort where we could show an overall stricture rate of 1,3%.

Changes in the text: We added the above mentioned study to the literature. Additionally we added the proportion of patients (1,3%) to the “Results” section (page 9, line 22) and complemented the “Discussion/Conclusions” section (page 11, line 15 and page 12, lines 15-19).

Comment 8: The case descriptions could use a bit more clarity and organization – it might be useful for the authors to arrange a description of the 2-3 cases per procedure type into their own paragraphs for easy comparison. Additionally, a table might add additional clarity as a summary of demographic, medical, and surgical information across procedure types/patients.

Reply 8: We appreciate the reviewer’s advice and added Table 3 to the main text.

Changes in the text: You can find the changes in the text on page 10, lines 20-21 and on page 17, line 18-20. Please also find the new table 3 in the appendix.

Comment 9: When accounting for cost, it might be useful to also comment on “time” – either time spent doing the procedure itself and/or any recovery time the patient spent in the hospital following the procedure.

Reply 9: We fully agree to the reviewer’s comment on the cost aspect in our manuscript. We decided, not to address healthcare economic aspects in the current setting and deleted the relevant passages from the text.

Changes in the text: We deleted the relevant passages from the text in the “Results” section and the “Discussion/Conclusions” section on pages 10 and 12.

Comment 10: On this note, if cost is the main reason to use LUC over URS, this should be mentioned in the introduction.

Reply 10: See reply to comment 9.

Changes in the text: See reply to comment 9.

Comment 11: Although I realize that the objective of this study was to specifically identify whether stone extraction with LUC is associated with a higher frequency of ureteral strictures, noting other complications or group comparisons would be warranted? That is, clinically, it would be relevant for the authors to comment on additional complications that should also be considered when concluding broadly that this procedure is effective compared to p-URS and l-URS). For example, the authors mention in their discussion that LUC is an effective procedure to URS with stone free rates from 87-93% as previously reported – do they see that in their patient cohort? The authors also allude to follow up rates being of interest, but do not mention this in their results.

Reply 11: The aftercare of all patients includes routinely performed ultrasound investigations during the first six months after stone removal. Thereafter annually ultrasound was performed for another three years.

We fully agree that asymptomatic patients may be disadvantaged when ureteric strictures appear at a later time. Consequently this patient group may be underrepresented in our study. We integrated this circumstance as a possible limitation into the text.

The stone free rates in the present cohort at first attempt were 91.4% (p-URS), 91.7% (l-URS) and 92.6% (LUC). These results are in line with previously reported studies.

Changes in the text: We enclosed the schedule of routinely performed ultrasound investigations in the “Methods” section (page 7, lines 19-21) and in the “Discussion/Conclusions” section (page 13, lines 3-6). We also enclosed a limitation comment in the “Discussion/Conclusions” section (page 13, lines 22-24).

We added a statement in the “Results” section on page 9, lines 5-6.

Reviewer B

Authors report a retrospective study of patients undergoing endoscopic intervention for distal ureteral stones. Patients underwent LUC or URS. Primary outcome was stricture rate based on upper tract dilation found on routine US. Stricture rates were low and similar across all groups. Authors conclude that LUC is effective in selected patients.

Comment 1: Were the procedures all elective? Or were some for urgent/symptomatic stones (other than those excluded for "severe pain" or infection)? If so this could have been part of the surgeon's consideration for which procedure to choose.

Reply 1: In our analyses we did not differentiate between elective and urgent procedures. As suggested by the EAU guidelines, we use to offer conservative treatment before performing

endoscopy (page 6, lines 3-5 in the main text), except for the above mentioned reasons. We modified the potentially irritating sentence in the main text.

We think, if there is an indication for interventional stone treatment, the urologist is supposed to perform primary stone removal in first attempt. During the intervention, surgeon's decision was decisively influenced by anatomic character of the urinary tract and the surgeon's experience. This, of course, excludes patients with signs of sepsis as in this situation, cure of infection is predominant in the order of treatment.

Changes in the text: We changed the sentence in the "Methods" section (page 6, line 5).

Comment 2: Please define the anatomic location of "distal ureter".

Reply 2: The entrance of the ureter into the small pelvis, visualized by crossing the iliopectineal line has proven to be the most reliable definition of the distal ureter. In detail, the present study refers to ureteric stones that also passed the crossover of the common iliac arteries.

Changes in the text: We gave details to the anatomic position of the stones in the "Methods" section (page 5, lines 10-11).

Comment 3: Were follow-up sonograms obtained based on a schedule? Only in symptomatic patients? Per the urologist's preference? If strictures were investigated only in those with symptomatic upper tract dilation, it may be possible that asymptomatic strictures (eg, partial or large caliber narrowing) were missed.

Reply 3: The aftercare of all patients includes routinely performed ultrasound investigations during the first six months after stone removal. Thereafter annually ultrasound was performed for another three years.

We fully agree that asymptomatic patients may be disadvantaged when ureteric strictures appear at a later time. Consequently this patient group may be underrepresented in our study. We integrated this circumstance as a possible limitation into the text.

Changes in the text: We enclosed the schedule of routinely performed ultrasound investigations in the "Methods" section (page 7, lines 19-21) and in the "Discussion/Conclusions" section (page 13, lines 3-6). We also enclosed a limitation comment in the "Discussion/Conclusions" section (page 13, lines 22-24).

Comment 4: The low event rate of stricture formation after endoscopic stone procedures is a considerable limitation. Authors should also consider whether the duration of follow-up (as low as 2 months) is sufficient to detect stricture. If yes, please justify within the literature.

Reply 4: We fully agree that the possible underrepresentation of patients with asymptomatic dilatation of the upper urinary tract is a limitation in our cohort. We enclosed this fact to the limitations section (see reply to comment 3). Concerning to the duration of follow-up: median follow-up time was 41 months and mean follow-up was 55 months. Only 21 of all 548 patients (3,8%) had a follow-up of 6 months or less. We find the overall follow-up period in the present study is sufficient, even notably longer compared to other studies. For example Perez Castro et al., included 9681 patients in their large multiinstitutional study of patients treated

ureteroscopically. The patients were recruited during the years 2010 and 2012, data was published in January 2014. Another large multiinstitutional study, including 11885 patients with urolithiasis was published by de La Rosette et al. January 2014. These patients were also recruited between 2010 and 2012 resulting in a follow-up less than we could show in our cohort. Darwish et al. prospectively analyzed 251 patients after ureteroscopic procedures and recommend a 12 months follow-up as sufficient for stricture and obstruction findings.

Fam et al. suggested a follow-up of 3 months after treatment of impacted calculi in a prospective analysis of 77 patients.

El-Abd et al. determined the incidence of symptomatic and silent obstruction after ureteroscopic procedures. In their multiinstitutional cohort they recommend a follow-up period up to 18 months for those patients with intraoperative complications. In our study, representing a follow-up of 41 months (median), the follow-up criteria by Darwish et al. and El-Abd et al. are met.

Stricture formation in the present study was 1,3% which is in line with the above mentioned studies, showing stricture rates of 0,6%, 1,5%, 1,9% and 7,8%. In the latter case, Fam et al. reported a cohort of 77 patients with impacted ureteric stones, possibly indicating a selection bias for postinterventional ureteric obstruction.

Changes in the text: We enclosed the schedule of routinely performed ultrasound investigations in the "Methods" section (page 7, lines 19-21) and in the "Discussion/Conclusions" section (page 13, lines 3-6). We also enclosed a limitation comment in the "Discussion/Conclusions" section (page 13, lines 22-24). We included the above mentioned literature into the manuscript.

Comment 5: The abstract conclusion of LUC being a "highly effective" procedure is not well supported by the primary data. Effectiveness data could include rates of failure/conversion (eg, failed LUC requiring conversion to URS). Suggest revising the conclusion to reflect the analysis that was performed.

Reply 5: We fully agree with this comment and changed the conclusion in the abstract.

Changes in the text: We changed the "Conclusions" section in the abstract (page 3, lines 2-4).

Comment 6: Authors also conclude that LUC is valuable in "certain circumstances." It would be helpful if these circumstances were specifically defined as part of the discussion alongside the primary data. If data are not adequate, then authors could suggest the conditions for LUC with the caveats of observational experience.

Reply 6: We are grateful for this important advice. To carry out an analysis of the surgeon's decision for a loop guided procedure is difficult in a retrospective setting. Our data does not include measurable parameters to objectify decision making. In fact, in a situation with a narrow ureteral orifice and a narrow or meandering ureter, surgeon's decision will rather be taken for a visualized endoscopic procedure. We will take that comment into account for performing a prospective analysis in the future.

Changes in the text: We added a statement in the "Discussion/Conclusions" section on page 11, line 25 to page 12, line 2 and on page 13, lines 13-15.