Peer Review File

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Reviewer A

1) General comments
This is an original article regarding with creating predictive model for evaluation of stone-left after fURS in upper ureteral stones. Mainly, we might suspect why you included only just upper ureteral stones. How about are distal, middle ureteral stones? The author should explain the reasons. In addition, there are some concerns about this study like below. Please note it.
Reply 1: Firstly, thanks to you for your review. The reason why we included only just upper ureteral stones is that the stone-free rate for other locations is high enough, close to 100%. It seems that there is no need to predict the stone free.

2) Comments for revisions
① Usually, if stone fragments were pushed back into renal collecting system during rigid-URS lithotripsy, the operator change to flexible ureteroscope and then try to remove it all again. Therefore, the left stone fragments are quite lower. Of course, it might depend on stone size, surgeon experience etc. Therefore, distance of the stone to UPJ in upper ureter is not relevant with stone free status. How do you think about its concern?
Reply 2-①: Yes, what you said, in the practice, is a standard process. The stones left in rigid-URS always are removed by secondary other procedures, like flexible ureteroscopy. However, it could only mean that the distance of the stone to the UPJ is not relevant with stone free status in the flexible ureteroscopy. The conclusion is not applicable to rigid-URS. Moreover, this further proves the importance of the surgical approach. In this study, patients which the procedures were switched to f-URS, were considered rigid-URS failures.

② With advancement of imaging study, can you find the stone volume by using 3D CT?
Reply 2-②: We appreciate your considerate advice. In regard to stone volume calculation, there are many methods in the published articles. We fully agree with you that the future of computing will be in the 3D space. The conclusion drawn from this will be more convincing, which had been presented in the text. However, our primary intentions are to reveal some characteristics easy to obtain and build an easy reliable model. The current most common way in which to express the size of stones is to give the maximum diameter of the stone in any measurable axis. In addition, 3D-reconstructed stone volume is not easy to get, and the equations differ in the different stone shapes, scalene, oblate, and prolate ellipsoid. We will carefully address the suggestion in the future study.

③ Stone shape you focused is interesting. However, the definition of stone shape is not comprehensive. Why did you define the criteria like between stone length and width not over 2cm? you should clarify about it. And then, how did you measure it?
Reply 2-③: Thanks to your positive comment and insightful suggestions. We have further

clarified the definition of stone shape in the text. We measured it in the maximum stone surface. We chose this criterion for the following reasons. Length and width are two factors that define the shape roughly. Without enough references, threshold of 2 cm was chosen because of that it showed a difference to the naked eye. It just a first attempt, since that there is not enough evidence for shape definition. We are always approaching the truth in constant exploration.
Changes in the text: "Length was the maximum diameter of the stone in any measurable axis and width was its orthogonal maximum diameter." (page 6, lines 92-93)

④ You measured the distance stone to UPJ. How did you measure it? What is the definition of UPJ portion?
Reply 2-④: we are sorry for our vague description and we have further clarified the measure method and definition of the UPJ in the text.
Changes in the text: "Distance of stone to the UPJ was the measured vertical difference from the stone center to the UPJ which was determined at the narrowest lower part of the renal pelvis in appearance." (page 6, lines 99-102)

Reviewer B

This is a retrospective, single-institutional study to assess the risk of non-stone-free. They found that stone length, shape(circle or oval), usage of flexible ureteroscopy, and distance from UPJ to stone, were associated with stone-free rate. Finally, they developed the nomogram to predict stone-free rate with these parameters.
To date, multiple studies have already developed the nomogram to predict the success rate of ureteroscopic lithotripsy. I wonder what was novel and at what point this nomogram was superior to other ones.
Reply: The novel and advantage point compared with other predictive models is its simplicity. All of the predictors are apparent characters. There is no need of further measurement or transformation. In addition, it does not rely much on advanced imaging.

Major point)
1. In the introduction and discussion, the authors said that factors which need CT scans are not useful in clinical practice. However, all the preoperative stone factors in this study came from CT images. I think measuring mean stone density is not so difficult.
Reply 1: We are sorry about our description perplexes you. What we said is that many current factors depend on digging into CT. For example, preoperative obstruction diagnosis, which was suspected to affect the stone free, was determined by density rate of different planes. We do not deny the important role of the CT in the stone procedures. It provides us many crucial references in clinical practice, just as the data for this study came from CT. In regard to the measurement of the mean stone density, we respect your opinion. As the saying goes, everyone thinks in his way. But it has to be said that the stone density does not change regularly.

2. The surgical procedure (rigid or flexible ureteroscopy) seems to be dependent on the

outcomes of the surgery. Physicians use flexible ureteroscopy because the upper tract stone was pushed back to the pelvis. Thus, including this factor is irrelevant to preoperative prediction.
Reply 2: As you said, some stones will be pushed back to the pelvis planned or unplanned. This phenomenon just shows that the rigid ureteroscopy is not suitable for some stones. In this study, retropulsion was defined as stone migrated up into the kidney out of design before disintegration, shown in page 6, lines 102-103. The data was obtained from clinical medical records. So, among circle stones which are suspected easy to retropulsion, direct flexible ureteroscopy might be more suitable.

3. in DCA, the authors should compare the nomogram and other previously established nomograms. Otherwise, we don't understand this nomogram is useful or not.
Reply 3: We appreciate your considerate comments. However, decision curve in this paper was generated to evaluate the net benefit of the model, indicated by the part above the two lines. The results showed that the model brought a net benefit in the range of probabilities between 10% and proximately 55%. Moreover, this study included three modalities in upper ureteral stones. To our knowledge, there is no similar study. We have no objective to compare with in the DCA.

4. There have been multiple nomograms to predict stone-free rates. (PMID: 23163835, PMID: 34173845, PMID: 30547902 and so on). The authors should discuss the difference and novelty of their results compared to previous ones.
Reply 4: Thanks to your helpful advices, and we have added the related comparison with other nomograms to highlight our contributions. A supplementary table 1 was also provided to highlight the difference. We will be glad to show it in the text if the editors permit.
Changes in the text: There were also many other prediction models. However, most of them were limited to one type of surgery, rigid or flexible ureteroscopy(15). Studies have demonstrated that the surgical methods can greatly affect the outcomes, four times of stone-left incidence of fURS less than URS in this paper. In addition, there were also lots of researches that includes all ureteral stones, which in our opinion was meaningless(16). Unless those rare stones, nearly all distal and middle ureteral stones can reach a high stone-free rate under standard skilled procedures. (page 12, lines 214-221)

Supplementary table 1: Comparisons between the model with others.

Item	Case	Center	Object	Surgery	Predictors	AUC	Validation
This model	**275**	**single**	**Upper ureteral**	**URS, URSard, fURS**	**Length, location, shape, surgery**	**0.803**	**Internal**
Imamura Y et al.	**412**	**Single**	**All ureteral**	**URS**	**Length, number, location,**	**0.743**	**Internal**

					pyuria		
Zhang Y et al.	348	Single	All ureteral, renal	fURS, miniPCN, microPCN	Surgery, location, irrigation, operation duration, stone mass	0.81	Internal
Hori S et al.	586	single	All ureteral, renal	fURS	Length, Hounsfield unit, location	0.845	Internal
De Nunzio C et al.	356	Double	All ureteral	URS	Number, size, distal ureteral location, hydronephrosis	0.75	Internal

5. all of the factor assessed (stone burden, hydronephrosis, and so on) should be included in table 1.

Reply 5: Thank you for considerate comments, and we have added those contents in the table1.

Changes in the Table 1:

Stone length(mm)	**11.5 ± 4.2**	**12.0 ± 4.3**	**0.511**
Stone width(mm)	**7.3 ± 2.4**	**7.7 ± 2.2**	**0.346**
Stone burden(mm^2)	**71.5 ± 45.8**	**78.2 ± 43.4**	**0.403**
Stone number	**247**	**37**	**-**
Stone density	**1239.6 ± 301.6**	**1265.8 ± 324.7**	**0.684**
Hydronephrosis (I/II/III/IV) ††	**5/141/59/33**	**0/24/8/5**	**0.817**
Surgery (URS/URSard/fURS) ‡	**99/86/53**	**26/6/5**	**0.004**
Stone to UPJ (mm)			**0.016**
≤30	**55**	**14**	
31-90	**137**	**22**	
>90	**46**	**1**	
Stone shape (quasi-circular/oval)	**76/153**	**18/17**	**0.039**

6. Because of the large difference in sensitivity of residual fragments between KUB and CT, it is inappropriate to mix the outcomes. Ideally, one measure should be used. At least, how many cases were assessed via CT/KUB should be described in table 1.

Reply 6: we fully agree with your comments. KUB and CT show a difference in sensitivity of residual fragments. However, for retrospective designed reasons, we cannot use one method throughout. We feel sorry that we did not record the number. This part

of the data would further clarify our research, so we add it into the limitation section. Changes in the text: Moreover, CT and KUB had a difference in sensitivity of residual fragments. (page 12, lines 227-228)

Reviewer C

The current manuscript describes the successful development of a simple nomograph to predict the stone-left after URS for proximal ureteral stones. It's based on a single-center, retrospective cohort in 2018, although the authors uniquely assess this predictive model focusing on only four parameters we can obtain from KUB X-ray. The result shows the accuracy of this model was high; however, this study has significant limitations and some points which need to be modified and clarified.
Reply: Thanks to your positive and insightful comments.

Major)
1) study-population
Considering the diversity of URS treatment, a single-center cohort may provide weak evidence which could apply for general practice. Therefore, adding other institutions' data should be preferable.
Reply 1: We cannot agree with your comments any more. High-grade evidence is our eternal goal. We are very glad to provide strong evidence if possible. However, for the time being, it is difficult to obtain complete data from other institutions. We feel sorry for that. In order to improve our evidence, we have tested our model in many ways. Once is there a chance, we will be happy to cooperate with other institutions.

2) methodology
While internal validation is a useful alternative tool, I couldn't understand why the authors simply validated this model with other cases. This study cohort was only in 2018, so they could have reassessed the model with the following year's cases or other institutions' data.
Reply 2: We greatly appreciate your positive comments. We have addressed your suggestion carefully. First of all, even reassessing the model with the following year's cases, it is still an internal verification. It just increases the number. Moreover, we cannot collect enough cases within three weeks. Though number of 275 cases in this study is not huge, it is enough for initial research. It can provide reference information for next multicenter prospective study. We are keen to receive recognition and will keep working for strong evidence. Thanks.

3) originality from prior studies
Several previous articles insist on their nomograms/ predictive models for URS. To elaborate the uniqueness and distinguish from those studies, I recommend providing the table comparing and highlighting the differences between this current study and others. Some were written in the discussion section; however, a visual summary better understands the impact of their result.
Reply 3: Thanks to your considerate suggestion. We have provided a supplementary table 1 following your advice. We are happy to present it in the text if the editors agree.

Change in the text: supplementary table 1 have been provided.

Supplementary table 1: Comparisons between the model with others.

Item	Case	Center	Object	Surgery	Predictors	AUC	Validation
This model	**275**	**single**	**Upper ureteral**	**URS, URSard, fURS**	**Length, location, shape, surgery**	**0.803**	**Internal**
Imamura Y et al.	**412**	**Single**	**All ureteral**	**URS**	**Length, number, location, pyuria**	**0.743**	**Internal**
Zhang Y et al.	**348**	**Single**	**All ureteral, renal**	**fURS, miniPCN, microPCN**	**Surgery, location, irrigation, operation duration, stone mass**	**0.81**	**Internal**
Hori S et al.	**586**	**single**	**All ureteral, renal**	**fURS**	**Length, Hounsfield unit, location**	**0.845**	**Internal**
De Nunzio C et al.	**356**	**Double**	**All ureteral**	**URS**	**Number, size, distal ureteral location, hydronephrosis**	**0.75**	**Internal**

Minor)

1) Why did the authors label the stone shapes into only two types (quasi-circular and oval)? Is there any scientific reason or literature?

Reply 1: To our knowledge, the effect of stone shape on SFR through the stone volume was reported. Shape on surface had not been reported. The criteria for stone shape were a preliminary attempt. We did not find any reference, but we will keep working for better evidence.

2) The 4mm size fragments detected by CT may be clinically significant. How about the median size of stones the authors treated in this study? I could not find the data in the result section nor Table 1.

Reply 2: Thanks for your review, and the data about the stone size has been shown in table 1.

Change in the text: Table 1:

Stone length(mm)	11.5 ± 4.2	12.0 ± 4.3	0.511
Stone width(mm)	7.3 ± 2.4	7.7 ± 2.2	0.346
Stone burden(mm^2)	71.5 ± 45.8	78.2 ± 43.4	0.403

3) The laser setting seems high power. How about pulse duration or mode like Moses effect?
Reply 3: The laser settings are based on operator preference, and we just recorded common range of use. Pulse duration has two fixed modes, dusting or fragmentation, and setting is not viable in all lasers, so we did not record it. Sorry about that. We fully agree with the improvement brought by the Moses effect in the stone procedures.

4)The authors should provide the stone composition data in the result section or a table since some stones are physically harder than others.
Reply 4: Thanks for your review, and the data about stone CT value have added in the table 1. Our primary aim is to reveal some easy predictors of postoperative stone free. It is hard to obtain the stone composition before the operation. On the other hand, extremely hard stones are rare.
Changes in the text: Table 1

Stone density	**1239.6 ± 301.6**	**1265.8 ± 324.7**	**0.684**

Reviewer D

General comments
The authors evaluate easily accessible risk factors attributing to stones left in the ureteroscopy in the treatment of upper ureteral calculi, and to build a simple and reliable predictive model. They concluded stones length, shape, modality, and distance of the stone to the ureteropelvic junction was significant factors on stones left and the risk of retropulsion was the shape of quasi-circular.
The reviewer generally agrees with the conclusion and it is a unique method to evaluate predictors of the possibility of a semi-rigid ureteroscopic approach to middle ureteral stones.
However, there are several issues need to improve. The reviewer would like suggests several issues as follows;
Reply: Thanks for your positive comments.

1) Specific comments for revision
a) Major
#1 What is the definition of upper ureteral stone?
Why did you include the patients that stones were located at lower ureter, such as 3 cm from the UPJ?
Reply 1: We are sorry about that, and the definition has been shown in the text. Stone located at 3 cm from the UPJ is still in the upper section, does not it? All of the included stones located at upper ureter, determined by imaging.
Changes in the text: Upper ureter extends from the ureteropelvic junction (UPJ) to the upper margin of the sacroiliac joint (or the lower margin of the fourth lumbar vertebra).

(page 6, lines 89-91)

#2 Hydronephrosis is not included in the patient background. The presence of hydronephrosis might be an important factor for operation result. Do you have any data on hydronephrosis?
Reply 2: Thank you for your reviewing, and we have added the information about the hydronephrosis in the table 1.
Changes in the text: table 1

Hydronephrosis (I/II/III/IV)	**5/141/59/33**	**0/24/8/5**	**0.817**

#3 How many cases of preoperative ureteral stents are there? Preoperative ureteral stent is also an important factor for operation result.
Reply 3: We agree with that preoperative ureteral stent is also an important factor for operation result. However, because of the retrospective design, there is a lot of missing data about it. We cannot judge it accurately. We are very sorry about that. We will pay attention to it in the further study. On the other hand, preoperative ureteral stent majorly improves the placement of the endoscopes.
Changes in the text: The information about the preoperative ureteral stent was unknown. (page 12, lines 228-229)

#4 CT value is an important factor for residual stone. How was it in this study?
Reply 4: We agree with your opinion. The data of the CT value has added in the table 1.
Change in the text: table 1

Stone density	**1239.6 ± 301.6**	**1265.8 ± 324.7**	**0.684**

b) Minor
#1 In this study, the exclusion criteria include narrow ureter cases.
Reply 1: Thanks.

#2 How do you measure the stone diameter in case of multiple stones?
Reply 2: Multiple stones were measured separately.

#3 Please add information such as stone diameter, number, location, and surgical technique in Table 1.
Reply 3: Thank you for your considerate comments. We have shown those data in the table1.
Change in the table1:

Stone length(mm)	**11.5 ± 4.2**	**12.0 ± 4.3**	**0.511**
Stone width(mm)	**7.3 ± 2.4**	**7.7 ± 2.2**	**0.346**
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Hydronephrosis	**5/141/59/33**	**0/24/8/5**	**0.817**

(I/II/III/IV) ††			
Surgery (URS/URSard/fURS) ‡	**99/86/53**	**26/6/5**	**0.004**
Stone to UPJ (mm)			**0.016**
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31-90	**137**	**22**	
>90	**46**	**1**	
Stone shape (quasi-circular/oval)	**76/153**	**18/17**	**0.039**

#4 Please, put together one figure that has (a) oval stone (b) quasi-circular stone.

Reply 4: Thank you for your considerate comment, and we have revised the figure following your comment. The figure is still presented as supplementary figure 1.

Changes in the text: supplementary figure 1.

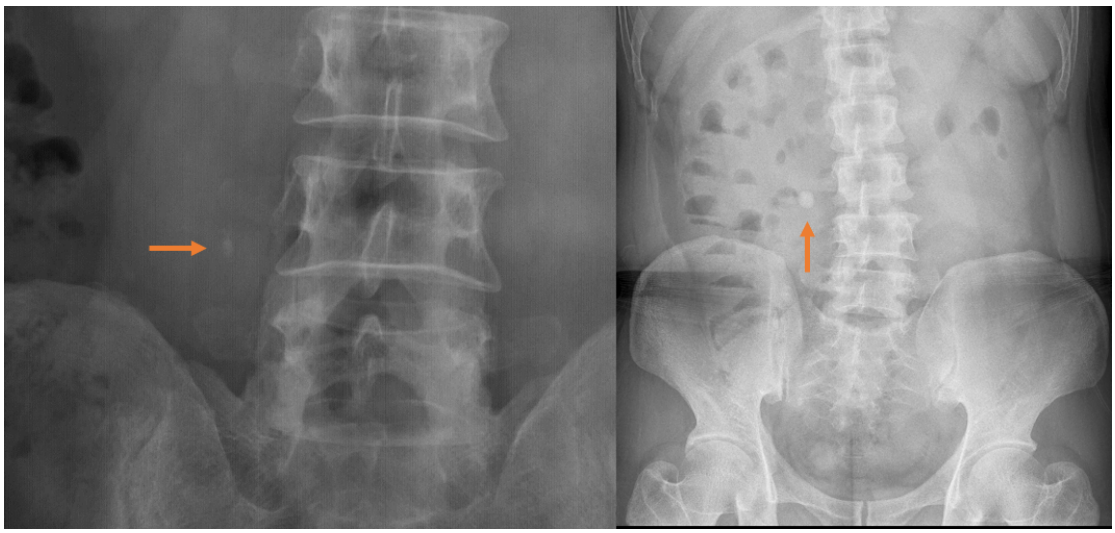

Figure 1: Profile of the two stone shapes. Oval (horizontal arrow), Quasi-circular stone (vertical arrow).