

Peer Review File

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Reviewer A

Congratulations on your description and presentation of outcomes. An interesting series, addressing a technique with paucity of data on long term outcome. I like the description of choosing which technique for different stricture sites which is informative and helpful to less experienced surgeons:

Comment 1: was rigid or flexible ureteroscopy used

Reply 1: Thanks for your question. In this study, we used F6/7.5 rigid ureteroscope (Richard Wolf, Knittlington, Germany).

Changes in the text: we added this information in text (see Page 8, line 141).

Comment 2: data on number of renal units, renal function (creatinine and GFR), previous history of UTI's, and baseline renal function if assessed by renogram

Reply 2: Thanks for your advice. The median preoperative serum creatinine and estimated glomerular filtration rate (eGFR) were 80.3 (11.4~212.0) $\mu\text{mol/L}$ and 94.8 (46.8~134.2) ml/min/1.73 m^2 , respectively. Sixteen patients had clear urinary tract infection (UTI) before operation. In fact, in our study, all patients have unilateral hydronephrosis, and most patients have been drained (nephrostomy or double-J stent) before surgery, and their renal function has been well saved before surgery. In addition, we have not performed renogram examinations for all patients, because most of the patients' conditions are clear. For example, we believed that the patient's renal function was good, if enhanced computed tomography (CT) showed significant enhancement of the renal cortex.

Changes in the text: we added this information in text (see Page 9, line 161-164).

Comment 3: what was the center using as means of follow up in the past? retrograde ureterogram, MAG-3 renal scan?

Reply 3: Thanks for your question. For patients after ureteral reconstruction with autologous onlay flap/graft, we focused on their subjective symptoms and imaging result. Patients with a nephrostomy tube underwent upper tract imaging urodynamics examination (IUE) after removing the double-J stent. Patients without a nephrostomy tube underwent cine magnetic resonance urography (MRU) after removing the double-J stent. The imaging examinations mentioned above can be referred to our previous research(1-3).

Changes in the text: none.

Comment 4: data on harvest site complications and bowel complications needs to be presented

Reply 4: Thanks for your advice. In our study, 13 patients underwent appendiceal onlay flap ureteroplasty, and there were no complications at the harvest site and other intestinal complications after surgery. In addition, 29 patients underwent lingual mucosa graft

ureteroplasty, and 4 patients (13.8%) had tongue numbness, which were gradually improved within 1 week after surgery.

Changes in the text: we added this information in text (see Page 9, line 168-172).

Comment 5: data on what intervention patient had before surgery (how many had nephrostomy tubes and how many had JJ stents, were any previous procedures performed?)

Reply 5: Thanks for your advice. In our study, nephrostomy was performed in 22 patients and double-J stent was indwelt in 10 patients, before their ureteral reconstruction surgery. In addition, there were 15 patients had previous management for ureteral strictures, including pyeloplasty, ureteroureterostomy, endoureterotomy and balloon dilatation.

Changes in the text: we added this information in text (see Page 9, line 164-168).

Comment 6: comparing laparoscopy vs. robotics for suturing nowadays is like comparing a bicycle to a car, if the robotic is readily available, then it is logically that robotics is superior so it is not really necessary to assess suturing with ureteroscopy as stated in the manuscript (invasive procedure risking the patient to investigate an unnecessary question)

Reply 6: Thanks for your comment. In the field of upper urinary tract reconstruction, repairing ureteral strictures with autologous onlay flap/graft was still a rare operation, especially using appendiceal onlay flap. The purpose of this study was to draw a conclusion through our practice and to advise urologists not perform ureteroscopy routinely for patients after ureteral reconstruction with autologous onlay flap/graft. For an innovative operation, we still have some questions before it was actually implemented. We believe that this was exactly the significance of our research.

Changes in the text: none.

Comment 7: More commonly people have described the act of passing a ureteroscope freely through a pyeloplasty repair as an objective measure. You need to reword/rephrase your objective of ureteroscopy as it sounds that you were assessing to see if it can replace ultrasound or MR, it is definitely complimentary if you find a stone or stricture on non-invasive imaging. It gives you visual evidence of patency but no functional data on obstruction like a MAG3 renal scan or dynamic ultrasound to assess ureteral jet etc.

Reply 7: Thanks for your comment. The conclusion of our research was, “patients after autologous onlay flap/graft ureteroplasty do not need to undergo routine ureteroscopy unless there is aggravation of hydronephrosis or other indications for ureteroscopy, such as stones”. We didn’t think that ureteroscopy can replace ultrasound or magnetic resonance imaging (MRI).

Changes in the text: none.

Reviewer B

This is a well-performed study on an interesting and less-evaluated medical condition. Indeed, the buccal mucosa graft can be used for the reconstruction of long ureteral strictures and recent reports have shown that it has better success rates and is associated with less perioperative complications.

The authors have shown that postoperative ureteroscopy is not mandatory and even increases risk of infectious complications. In my opinion, the article and the results are well prepared and can be interesting for the urologic community. The amajor threat of the study is its ethical component.

From the paper, it seems that the authors have performed ureterscopy without any clear indication. The authors have decided to examine the healing of the lesion with an invasion diagnostic modality, that could potentially damage the reconstruction site. Why should we perform any invasive procedure without any indication? If there are indications, please mention those and also state what were the selection criteria. Otherwise, the study seems to have ethical issues.

Reply: Thank you for your critical comment. This study approved by the Ethics Committee of Peking University First Hospital (ethical review number: 2019SR134). In fact, all patients have been indwelt double-J stents after ureteral reconstruction with autologous onlay flap/graft. We performed ureteroscopy to remove their double-J stents and observe the healing situation, 2-3 months after surgery. It was indeed an invasive operation, but as a result, valuable experience has been gained, which was conducive to formulating more reasonable management protocol. Changes in the text: we added this information in text (see Page 6, line 91).

Other comments are:

Comment 1. Introduction: Lines 80 to 90 refer to the methods and not introduction. I would recommend to delete them and modify accordingly the methods section.

Reply 1: Thank you for your advice.

Changes in the text: we have modified our text as advised (see Page 5, line 80 and Page 6, line 86-90).

Comment 2. Methods: can you provide ethical approval number. For me this study is problematic, and I believe in many centers it would be rejected due to ethical concerns.

Reply 2: Thank you for your advice.

Changes in the text: we added the ethical approval number in text (see Page 6, line 91).

Comment 3. Reporting the results in the methods section is not correct (lines 98-112). Please include those data in the results section.

Reply 3: Thank you for your advice.

Changes in the text: we have modified our text as advised (see Page 9, line 157-177).

Comment 4. In addition, the results be shortened. There is no need to repeat what is already written in the tables. Outline and write what is important.

Reply 4: Thank you for your advice.

Changes in the text: we have modified our text as advised (see Page 9, line 157-177).

Comment 5. How many patients were initially considered for this study and how many were finally recruited? How many were excluded and due to which factors?

Reply 5: Thank you for your questions. Because this was an observational study, we did not calculate the sample size at beginning. With the increase in the number of cases, we have gradually discovered that postoperative ureteroscopy may bring some adverse events to patients, while providing limited clinical value. Therefore, we terminated this observational study early and collected 27 patients who completed ureteroscopy. For not ureteroscopy group, 15 patients who had undergone ureteral reconstruction surgery for more than 6 months were recruited and 5 patients less than 6 months after surgery were excluded. In fact, ureteroscopy was performed

for patients after ureteral reconstruction with autologous onlay flap/graft routinely. After we have done enough 27 cases, we terminated. Therefore, the follow-up time of patients in the ureteroscopy group was both more than 6 months. Follow-up for more than 6 months was more convincing for us to evaluate the success rate of ureteral reconstruction surgery.

Changes in the text: none.

Comment 6. The authors state that the objective success rate was the absence of the obstruction on the imaging. What was the imaging? What was considered as the absence of the obstruction? Please clearly state the how the success was defined Was it performed before or after ureteroscopy? If no problems were identified with the imaging, why the authors performed the ureteroscopy.

Reply 6: Thank you for your questions. For patients after ureteral reconstruction with autologous onlay flap/graft, we focused on their subjective symptoms and imaging result to judge the success rate of the operation. Patients with a nephrostomy tube underwent upper urinary tract imaging urodynamics examination (IUE) after removing the double-J stent, 2-3 months after surgery. Patients without a nephrostomy tube underwent cine magnetic resonance urography (MRU) after removing the double-J stent, 2-3 months after surgery. The imaging examinations mentioned above can be referred to our previous research(1-3). We performed ureteroscopy to remove their double-J stents and simultaneously observe the healing situation. Therefore, ureteroscopy was performed before imaging examination.

Changes in the text: none.

Comment 7. The authors state "We used the success rate of repair surgery to indirectly reflect the clinical significance of ureteroscopy" (line 212-213). I cannot understand the meaning. The authors had 100% success rate.

Reply 7: Thank you for your comment. To be honest, this sentence is indeed unclear. We believed that the clinical significance of performing ureteroscopy should be evaluated. In addition to allowing us to observe the appearances of autologous onlay flap/graft, ureteroscopy may affect the success rate of ureteral repair surgery. The first hypothesis was that the success rate of ureteral repair surgery was decreased as the ureteroscopy was an invasive examination. The second hypothesis was that the ureteroscopy can detect poor healing of the autologous onlay flap/graft in time which allow us to deal with it in time to avoid more serious situations. We defined the objective success criteria as patency of the ureter and no hydronephrosis or mild hydronephrosis at 6 months postoperatively. The objective success rate of the two groups was both 100%, which mean that ureteroscopy has no effect on the success rate of ureteral repair surgery.

Changes in the text: we have modified our text (see Page 11, line 212).

Comment 8. What is the subjective success rate, please define it. If it is based on patients evaluation, have the authors used any standardized tool , to assess the improvement of the symptoms.

Reply 8: Thank you for your questions. Subjective success was defined as the resolution of flank pain without a double-J stent and nephrostomy (see Page 8, line 142-143). In fact, we only followed up patients for flank pain and did not use any standardized tool to quantify this subjective feeling.

Changes in the text: none.

Reviewer C

The paper is appropriate for submission in the Translational Andrology and Urology. Authors report the initial experience of a center in analyzing the safety and clinical significance of performing ureteroscopy after ureteral reconstruction with autologous onlay/graft.

Congratulations for the work in this paper.

The conclusion of the study is expected, as it is certain that only patients with any sign/symptom or non-invasive exam that suggest a complication should undergo ureteroscopy. Despite this, the study was well conducted and the article is well written.

The images are very good and illustrative. Tables are ok.

The paper have some limitations and biases cited in the end of the discussion.

Suggestions:

(Line 233-237) It is not necessary to cite this method-related statement again in the discussion. How long after revision ureteroscopy was the double-J catheter removed? And how was it removed?

Reply: Thank you for your comments. After the ureteroscopy, a new double-J stent will be indwelt for one month, and then it would be removed through the cystoscopy.

Changes in the text: we have modified our text as advised (see Page 12, line 232).

Reviewer D

Thank you for the authors' excellent effort in managing these complex ureteric stricture conditions.

From the clinical interest point of view, the results would be more meaningful if the manuscript focuses on the comparison between different reconstruction techniques, rather than a comparison between the groups with or without ureteroscopy performed. Furthermore, ureteroscopy has not been a routine investigation in post-ureteric reconstruction patients in many centres. The message on the optional use of ureteroscopy after reconstruction can be brought out as an integral part of the discussion of the results.

Reply: Thank you for your comments. We will continue to work on the field of upper urinary tract repair, including surgical techniques and clinical research.

Changes in the text: none.