

Peer Review File

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Reviewer A

The most interesting question to me is whether peristalsis affects the function of the ideal ureter. Unfortunately, this paper can't address that question, because the only patients who had the Whitaker test done in this population were the ones who were still symptomatic (lines 60-61):

“The Whitaker test was performed before removing a nephrostomy catheter at 3 months after the surgery in patients who still had symptoms or no relief of hydronephrosis,”

Getting Whitaker test in asymptomatic patients would be quite helpful.

Response: Thank you for pointing out our shortcomings and giving valuable suggestions. Initially, the purpose of the Whitaker test was to provide evidence for suspicious patients to pull out the nephrostomy tube or ureteral stent. Therefore, the enrolled patient was symptomatic. Of course, this caused the lack of asymptomatic groups as a comparison. To make further investigation, we expanded the MRU examination to 42 cases, and 20 cases had Whitaker test results simultaneously. The Whitaker test was not limited to those with symptoms.

Changes in the text: We expanded the number of cases and re-analyzed the parameters of peristalsis in cine MRU. We listed the changes one by one below.

It's not surprising that some of these patients with symptoms had narrowings at the anastomosis. Only 2/8 had any issues with peristalsis (“slow”) and both of these had normal Whitaker tests.

In a robust study, all patients and not just the symptomatic ones would have had pressure and peristalsis quantified, so that the true significance of slow peristalsis could be determined.

Response: Thank you for the valuable comments! We have expanded the number of cases in those who had a nephrostomy tube as a ready-made channel for the Whitaker test. Whitaker test is invasive for patients without nephrostomy, so we did not perform the Whitaker test on such patients. Thus, a total of 42 patients underwent cine MRU, and 20 of them finished the Whitaker test successfully.

In order to investigate whether peristalsis affects the function of ileal ureter, we compared the amplitude, contraction rate, peristaltic frequency, ureteral jets, and peristaltic efficiency in

the elevated pressure and the normal pressure group. An interesting finding is that slow peristalsis does not affect the function of the ileal ureter. On the contrary, patients with more peristaltic frequency, larger amplitude, but lower peristaltic efficiency had a poor function of transporting urine.

Patients in the elevated pressure group had larger amplitude (13.80 ± 5.73 mm vs. 8.09 ± 3.38 mm, $p=0.024$), higher contraction ratio [0.68 ($0.59-0.79$) vs. 0.59 ($0.25-0.79$), $p=0.028$], more peristaltic waves [7 ($6-8$) vs. 4 ($3-8$), $p=0.025$], but lower peristaltic efficiency [0.50 ($0.29-0.50$) vs. 0.75 ($0.33-1$), $p=0.029$] compared to the normal pressure group.

Furthermore, patients with slow peristalsis had a normal pressure in the Whitaker test. So we believe that peristaltic efficiency is the most important evaluative indicator in cine MRU. The frequency and amplitude of peristalsis do not really affect its function. The reason may be that the rhythm of the ileal graft is innervated by the autonomic nerve. The autonomy allows it to maintain the basic peristaltic frequency, and the intestinal contents can stimulate peristalsis, so the frequency and amplitude of peristalsis increase when urination difficulty exists. [Silbernagl S. Color Atlas of Physiology 7th Ed.[M]. China Science and Technology Press, 2015.]

esophageal sphincter opens (→ A4). A peristaltic wave forces the bolus into the stomach (→ A5, B1,2). If the bolus gets stuck, stretching of the affected area triggers a secondary peristaltic wave.

Changes in text:

In the Methods section,

- (1) Add the statistical method (Kolmogorov-Smirnov test) for whether the variables are normally distributed. (Page 6 Line 123-124)
- (2) The comparison of renal function before and after surgery was revised, and the paired t-test was used. (Page 6-7 Line 124-126)
- (3) Add the statistical methods that compare the cine MRU parameters between the high-pressure group and the low-pressure group. (Page 7 Line 126-131)

In the Results section,

- (4) Update the number of cases of MRU and Whitaker test in the Results. (Page 7 Line 134)

(5) The correlation analysis results of MRU parameters and postoperative creatinine or eGFR were added to the results. (Page 7-8 Line 146-147)

(6) Add the comparison of MRU parameters and postoperative renal function between the high pressure group and the low pressure group, and revise the Table 2 to list the detailed results of the comparison between the two groups. (Page 8-9 Line 164-173)

(7) Add the detailed results (cine MRU and Whitaker test) of the newly added cases to Table 3 and move it to the supplementary. (Page 9 Line 174, Supplementary Table)

In the Discussion section,

We added the reasons and enlightenment for the active peristalsis and poor efficiency of peristalsis in the high-pressure group. (Page 11 Line 225-227, Page 11 Line 232-233)

Reviewer B

The topic of study is novel and interesting. However, there are some issues which needs to be addressed:

1. Baseline characteristics and results

a] are all the surgeries done by the same surgeon or a team of surgeons utilizing the same technique. Widely different techniques may have different outcomes.

Response: All the ileal ureters were performed by the same surgeon, and the technique was reported in the previous study [*Zhong W, Hong P, Ding G, et al. Technical considerations and outcomes for ileal ureter replacement: a retrospective study in China. BMC Surg. 2019;19:9*].

Changes in the text: We have added descriptions of surgeon and techniques in Materials and Methods. (Page 4 Line 65-66)

b] based on MRU - it will be good to measure the length of the ileal conduits? are there differences between the high pressure and low pressure group (by Whitaker) in terms of the ileal interpositional length used?

Response: Thank you for your suggestion. The length of the ileal ureter was measured in the MRU image by curving tool in PACS work station. We compared the length in the low-pressure and high-pressure groups (22.32 ± 5.03 mm vs. 26.15 ± 3.47 mm) and found no statistical

difference ($p=0.224$).

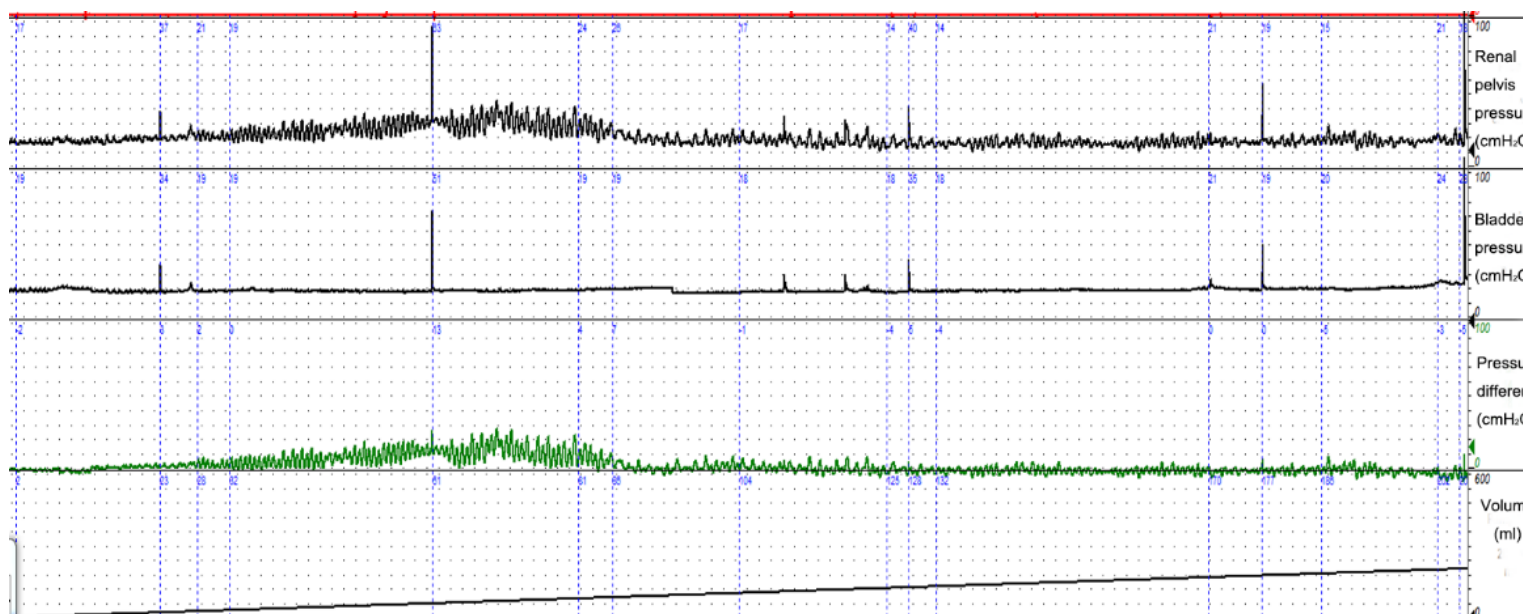
Changes in the text: We clarified the measuring method based on MRU. (Page 5 Line 96-98)

Add the length of the ileal conduits to the Results, as well as the difference between the high pressure and low pressure group. (Page 7 Line 139, Table 2)

c] Figures 1 and 2 shows MRU pictures in which the bladder is full. Whitaker tests require bladder to be emptied with an indwelling catheter (I note that the bladder pressure is constant on Figure 3 but pressure readings not visible and in Fig 3, the bladder IS empty). Please clarify if the comparisons or measurements of the MRUs are done with a full or empty bladder. In addition please explain how the diameter lengths are standardised is it along certain bowel markings or perpendicular to the direction of the bowel. It does seem subjective. However, I agree that amplitude and peristaltic waves are more objective.

Response: The protocols of cine MRU and Whitaker test are different. During MRU, the patient needs to hold back the urine (full bladder). Because it is more convenient to observe the presence or absence of reflux and the condition of the urinary tract under urine load when holding the urine. In the Whitaker test, the catheter is placed in advance and the pressure is adjusted to zero to ensure that the contrast agent can enter the bladder smoothly. Therefore, unless there is urethral obstruction, the bladder pressure can remain stable (coughing and other actions that increase abdominal pressure can affect bladder pressure).

Do you mean the pressure reading in **Fig 4**? In the original image, the readings can be seen clearly. It may be due to the convenience of reviewing the manuscript, the uploaded image is compressed. We have pasted the original image of Fig 4c below.



The diameter of the ileal graft is perpendicular to the direction of the bowel. Taking into account the different baselines of the intestine caused by personal factors, we use the contraction rate to minimize this bias. In addition, we have 2 radiologists majoring in the urological subgroup to evaluate cine MRU parameters separately, and the final results were averaged to reduce human error.

Changes in the text: We add the brief protocol of cine MRU and Whitaker test to the method. (Page 4-5 Line 80-89)

We explain how the diameter lengths are standardised in the method. (Page 5 Line 99)

d) For table 3, can the readings be compared between the high and low pressure groups? Unfortunately only 9 of the patients had the whitaker tests which may limit the interpretations.

Response: We have increased the number of cases for the Whitaker test to 20 cases and compared the MRU parameters between the high and low pressure groups. We found that patients in the elevated pressure group had larger amplitude (13.8 ± 5.7 mm vs. 8.0 ± 3.4 mm, $p=0.022$), higher contraction ratio [0.68 (0.59-0.79) vs. 0.59 (0.25-0.79), $p=0.028$], more peristaltic waves [7 (6-8) vs. 4 (3-8), $p=0.025$], but lower peristaltic efficiency [0.50 (0.29-0.50) vs. 0.75 (0.33-1), $p=0.029$].

Changes in the text: We revised the Table 2 and compared between the high and low pressure groups. (Table 2, Page 9 Line 164-171)

2. The Whitaker test assesses for obstruction along the entire length of the reconstructed urinary tract - most likely at proximal and distal anastomosis. However, the cine MRU evaluates for obstruction likely distally at the distal obstruction. Can the authors please comment on this?

Response: The Whitaker test not only shows the reconstruction of upper urinary tract image, but also evaluates obstruction by sensitive pressure changes. It can be observed that the proximal end is dilated, the distal end is unclear, and the pressure increases with the perfusion when urine/contrast agent accumulates in the renal pelvis and proximal ureter. In contrast, cine MRU focuses on the peristalsis of the intestine and the result of peristalsis (ureteral jets). Although not as sensitive as pressure changes, seeing the ureteral jets is strong evidence for the reconstruction of urinary tract patency. The regular and effective peristalsis of the intestine is the guarantee for spouting. Therefore, cine MRU can be competent to evaluate the process and results of the reconstructed upper urinary tract. In addition to the dynamic images of the cine MRU, the conventional T1WI, T2WI sequence can evaluate the proximal and distal anastomoses. In general, the results of the Whitaker test are more intuitive, while MRU requires a certain foundation of imaging and MRI reading.

Changes in the text: We added the respective characteristics of cine MRU and Whitaker test in obstruction evaluation. (Page 10-11 Line 212-219)

3. It is crucial for the authors to define better how their study can translate into clinical practice real life. The Whittaker test is tedious and is dependent on the PCN tube (only 9 of the patients did the PCN) ; hence realistic to do it only once after the initial surgery. The cine MRU is repeatable and hence can be use to evaluate ileal interposition pressures months or years subsequent to surgery. If both needs to be done for interpretation, then this is not realistic.

Response: The biggest limitation of the Whitaker test is the establishment of invasive channels. Therefore, we do not recommend that patients without a nephrostomy tube receive a nephrostomy just because of this examination. This study adds evidence for the relationship between pressure and bowel peristalsis in patients with ileal ureter replacement. We found that the peristaltic efficiency in cine MRU is a more important indicator. As our answer to your second question, the results of different sequences such as cine MRU and T1WI, T2WI can be

used to evaluate the reconstruction of the upper urinary tract in detail. Therefore, we recommend cine MRU after ileal ureter replacement as a routine examination, and the Whitaker test as a supplementary examination to clarify equivocal cases.

Changes in the text: In the last paragraph of the discussion, we added a summary of the clinical application of MRU and Whitaker after ileal ureter replacement. we recommend cine MRU after ileal ureter replacement as a routine examination, and the Whitaker test as a supplementary examination to clarify equivocal cases. (Page 13 Line 273-278)

4. Noting point 2 above and the average the median measurements of amplitude and contraction ratio were 9.2 mm and 0.62, respectively, what would the authors evidenced based cut off points?

Response: We want to show that the ileal ureter is wider than the normal ureter and cannot be completely contracted to close to form a bolus. The amplitude and contraction rate may look good, but the urine is not actually transported. This leads to the importance of the efficiency of peristalsis below.

Changes in the text: We rearranged the order of the peristaltic characteristics of the normal ureter and the ileal ureter in the discussion. It shows that the peristalsis and amplitude of the ileal ureter cannot be evaluated only, which leads to the discussion of peristaltic efficiency below. (Page 11 Line 224-227, Page 11 Line 230-231)