Author's response to reviews

Title: Ureteral reconstruction using a tapered non-vascularized bladder graft: an experimental study in a canine animal model

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Author’s response to reviews:

For Reviewer #1:

1. The reasons why we selected the beagle in out study included good compliance for the experimental surgery and resistance to infection. Besides, we also considered the different growth rate between pigs and dogs, which meant that the porcine model would gain much more weight and larger size during the follow-up. This may result in heterogeneity at the end-point of study. Actually, we have explored the porcine model recently, looking forward to validation to our previous study.

2. The ureteral stent was maintained for the postoperative 6 weeks and removed through a brief cystostomy. (Methods, Paragraph 5, Line 5) The retrograde urography was performed 2 weeks later.

3. The main purpose of this study was to evaluate the anatomical possibility of our novel substitute for ureteral reconstruction. The current result verified that the free graft was survivable in 8 weeks after the surgery, and theoretically the time for neovascularization was adequate to maintain subsequent nourishment. Longer follow-up period can be and has already been designed to assess long-term results and complications (for example, ureteral stricture), which were not included in the purpose of this study.
4. We are so grateful for what the reviewer recommended. Actually, assessment for blood flow has just included in our latest study. However, we believed that the current results, including the nutrient vessels and the surviving state of the graft, were sufficient to indicate its possibility. Long-term results have already been considered for evaluation of patency.

5. According to our pathologists, the partial loss of urothelial lining was quite slight and local. Even in the denuding area, the basement membrane was complete so as to develop new urothelium. Moreover, we believe that the reviewer also cannot deny the possible effect of "retrograde catheterization and instillation of the contrast agent" leading to denuding of the urothelial epithelium.

6. Still very grateful for the recommendation. However, in our opinion, the completeness of the urothelium was a direct evidence proving the viability, and the staining for apoptosis would certainly be a good alternative.

7. It is reiterated that the main purpose of this study was to evaluate the anatomical possibility of our novel substitute for ureteral reconstruction. By “anatomical possibility” we meant not only its surgical feasibility but capability for blood supply establishment, relative to “functional possibility”. It is unlikely to develop leakage after 8 weeks. The long-term patency, which will influence the split renal function, should be followed up as a part of functional assessment.

For Reviewer #2:

1. Although the practice of Monti and Mitrofanoff techniques is quite mature, it is still possible to develop specific postoperative complications due to the application of intestinal substitute. The purpose for what we established the animal model was to explore the substitute material with urothelial lining and meantime avoid intestinal interference. (Modified in Introduction, Paragraph 2 and Discussion, Paragraph 2)

2. In most of our references, the beagle was involved as animal model. The anatomy and the histology of the beagle ureter and bladder are quite similar with human beings, including the blood supply of ureter. The beagles and human beings have a comparatively similar bladder capacity regarding to their own weight. In our study, the postoperative bladder capacity was not evaluated, though “no obvious sign of persistent frequent micturition or other alteration of micturition rhythm was observed”. (Modified in Discussion, Paragraph 6)

3. The beagle usually grows up into adulthood at 10 to 12 month old. A 1-year-old beagle is a young adult dog with relatively stable weight and ideal physical quality, which are important for the study design and surgical procedure. (Modified in Methods, Paragraph 1)

4. The number of animal case in most of our references was approximately 8-12. Without a control group, we believed that the results based on 9 cases was sufficient for our preliminary conclusions.
5. In clinical practice, a stent is usually maintained for 1-3 months after ureteral reconstruction, according to the severity of injury and the surgical procedure. However, the main purpose of our current study was assessment of the surviving state of the graft. Thus, the stent duration of 6 to 8 weeks was enough.

6. The mild hydronephrosis probably resulted from urine reflex due to the ureteral stent. “The urography indicated patent urine excretion and normal ureteral caliber, without obvious fistula or stenosis.” (Modified in Discussion, Paragraph 5)

7. The main purpose of this study was to evaluate the anatomical possibility of our novel substitute for ureteral reconstruction. Although the results in mid-ureter can theoretically be repeated in proximal ureter, this suggestion should be taken. We also mentioned in the Discussion section that “The potential clinical application of this procedure is reconstruction of defect and stricture in upper and mid-ureter”.

8. The Discussion section have been improved according to the replies above.

9. It will be more interesting to compare our technique with other traditional ones. Also, it is possible to do so. However, we drew a conclusion focusing on the substitute material with urothelial lining and without interference to intestine, which were our advantages. The comparison will not make the point “much more strong”.

10. As mentioned in the Methods section, we used H.E. in figure 3 and 4. (Modified in Figure Legend)