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ORIGINAL PAPER

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Covering of the terminal ureter with de-serosalized muscle layer of the ileum for antireflux ureteroileostomy: an experimental study in dogs and a preliminary clinical trial

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Abstract We demonstrated a new operative technique for antireflux ureteroileostomy in dogs. The severed ureter was reimplanted into the isolated ileum. Ten terminal ureters were covered with a 2×2 cm^2 section of de-serosalized ileal wall after direct ureteroileostomy, and another six terminal ureters were covered with a 2×2 cm^2 section of non-de-serosalized full-thickness ileal wall. Thirteen ureters were directly anastomosed to the ileum without any additional procedures. The bladder was augmented by the detubularized ileum with the ureter. Postoperative evaluations on ureteral stenosis and reflux were performed monthly for 3 months. The ureters covered with the de-serosalized ileal wall prevented ureteral reflux even when the intravesical pressure climbed as high as 100 cm H_2O. Although two of these ten ureters demonstrated strictures at the precise site of direct ureteroileostomy, the sections of the ureters covered with the de-serosalized ileal wall were opened and did not collapse. In the resected specimens, the terminal ureters were found in the intramural part of the ileum. The ureters covered with the full-thickness of ileal wall did not prevent reflux. Our method of covering the terminal ureter with the de-serosalized ileal wall worked well as an antireflux mechanism, and the intramural ureter did not cause ureteral stricture. After this animal experiment, we introduced this antireflux mechanism clinically.

Keywords Ureteroileal anastomosis · Antireflux technique · De-serosalized ileum · Continent urinary diversion · Orthotopic ileal neobladder

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Introduction

The ileum has been commonly used for many types of urinary diversion. Although it remains controversial whether reflux actually needs to be prevented in the low-pressure reservoir, the belief that reflux of the ureteroileal anastomotic site is harmful to the kidneys has led to the widespread use of antireflux ureteral reimplantation into ileal pouches (11). Postoperative ureteral stricture at the site of ureteroileostomy is a troublesome complication after urinary reservoirs are formed using the ileum. Although several antireflux ureteroileal anastomotic methods have been designed and clinically used (2, 6, 13, 18, 21), no method has achieved the absolute prevention of postoperative ureteral stricture.

Ureteral stricture following antireflux ureteroileostomy is one of the most serious complications in ileal neobladders. Some patients with anastomotic ureteral strictures have received nephrostomy or ureteral reimplantation because of the difficulty of endoscopic repair of the ureteral strictures (9, 14, 17). To resolve this problem, an antireflux ureteroileal anastomotic technique without stricture has been awaited as a mean to form ileal neobladders safely.

The cause of ureteral stricture following antireflux ureteroileostomy has not been clarified. Recently, some studies have reported that the most widely used technique for ureteroileostomy, the Le Duc method, caused postoperative ureteral strictures in 1.5 to 29% of patients who underwent ileal neobladder (5, 9, 14, 21). In the Le Duc method, the ureteral adventitia is not covered with the ileal mucosa and the intraluminal ureter stays in contact with the urine after surgery until epithelization over the intraluminal ureter is spontaneously completed. Inflammatory scarring at the intraluminal ureteral wall resulting from urine contact with the ureter might cause ureteral stricture using this technique (13). Animal experiments performed by Abol-Enein et al. showed that inflammatory scarring of the ureteral wall occurred when the ureteral adventitia was exposed to the urine during

the early postoperative period (3, 4). They emphasized the need to completely cover the ureter with the mucosa and also the need for a definitive anastomosis between the ureter and the ileal mucosa to prevent postoperative ureteral stricture.

After performing an antireflux ureteroileal anastomosis with complete covering of the introduced intraluminal ureter with the ileal mucosa over a length of 3 cm, Wenderioth et al. reported that the rate of ureteral stricture at the reimplantation site was 8% at 1–36 months follow-up (21). On the other hand, Schwaibold et al. achieved a postoperative ureteral stricture rate of 3% after performing a modified Le Duc method that diminished the length of the intraluminal ureter without mucosal covering. (19). The experimental study performed by Abol-Enein and the clinical reports on antireflux ureteroileostomy indicate that ureteral stricture cannot be completely prevented merely by protecting the ureteral adventitia from urine contact.

To prevent ureteral stricture after antireflux ureteroileostomy, the ureteral adventitia should be protected from urine and definitive anastomosis between the ureter and ileal mucosa should be performed. We hypothesized that postoperative ureteral stricture may be prevented by loosening the periureteral tissues when performing the complete mucosal covering and definitive anastomosis described above. We performed a new technique in dogs based on the principle of the complete and loose covering of the terminal ureter. In this technique, the ileum was de-serosalized to cover the ureter loosely and the terminal ureter was placed outside the ileal lumen to prevent urine contact with the ureteral adventitia. We describe the operative technique and the results of our animal experiment, as well as report the first use this technique for a clinical case.

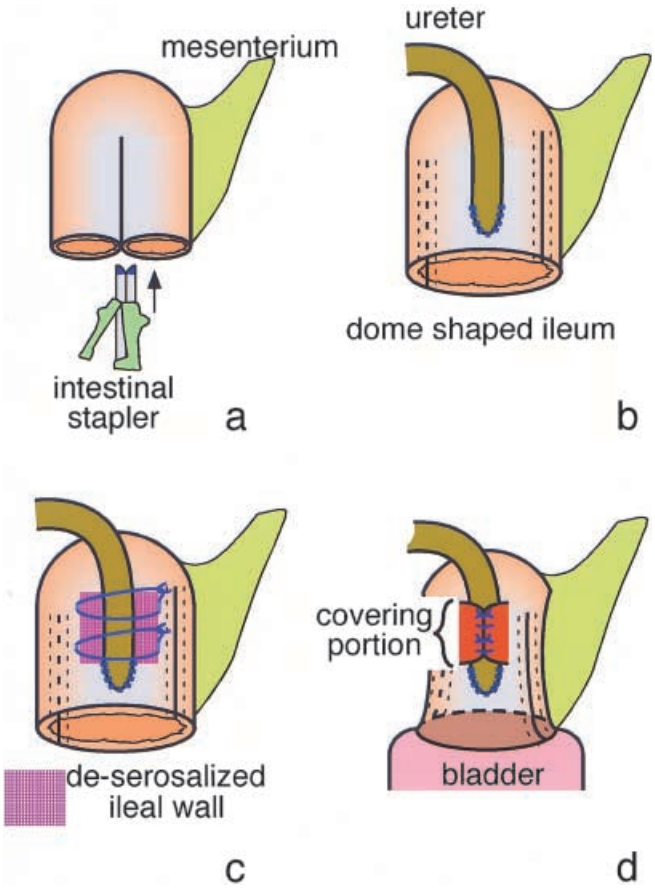

Fig. 1 **a** Each medial side of the U-shaped ileum is conjoined. **b** Direct ureteroileostomy is performed. **c** A 2×2 cm^2 of the ileal wall is de-serosalized. **d** The terminal ureter is covered with de-serosalized muscular layer of the ileum, and the ileal dome is anastomosed to the bladder

Materials and methods

A total of 15 female mongrel dogs, weighing 10.5–22 kg, were used for these experiments. The surgical procedures were carried out under general anesthesia with thiopental sodium. A segment of the terminal ileum measuring 15 cm in length was isolated and formed into a dome shape using an intestinal stapler (Fig. 1a). The ureter was severed at the ureterovesical junction. The first 5 mm of the distal end of the ureter was spatulated, and then a direct end-to-side anastomosis between the ureter and the ileum was performed using 5–0 poliglecaprone sutures (Fig. 1b). A total of 29 ureters were reimplanted into the ileal dome, bilaterally in 14 dogs and unilaterally in one. Two types of antireflux procedures were added to the direct ureteroileostomy in 16 ureters. The remaining 13 ureters did not receive any additional antireflux procedures.

A 2×2 cm^2 section of the ileal wall at the cranial site of the ureteroileostomy was de-serosalized by peeling off the serosa using a pair of forceps (Fig. 1c). Hemostasis on the de-serosalized surface was achieved by direct pressure and electrodiathermy. To cover the extraluminal terminal ureter with the de-serosalized muscle layer, the bilateral longitudinal edges of the de-serosalized area were sutured together over the terminal ureter using 3–0 polydioxanone sutures (Fig. 1d). A 2-cm section of the terminal ureter was completely covered with the de-serosalized ileal muscle layer (type A antireflux method). Ureteroileostomy with this method was performed on ten ureters.

A 2×2 cm^2 full-thickness section of ileal wall was used to cover the terminal ureter. The bilateral longitudinal edges of the 2×2 cm^2 area were sutured together in the same manner used for the type A method, and the 2-cm section of the terminal ureter was covered with the full-thickness ileal wall (type B antireflux method). Ureteroileostomy with this method was performed on six ureters.

The dome shaped ileal segment with the reimplanted ureters was anastomosed to the incised bladder using 3–0 polydioxanone sutures (Fig. 1d). All ureters were stented by a 4 Fr ureteral catheter, and a 12 Fr urethral catheter was indwelled into the bladder. These catheters were removed within 2 weeks after the operation. Prophylactic antibiotics were given for 3 days postoperatively.

Postoperative evaluations were performed under general anesthesia. Retrograde cystography was performed for the evaluation of ureteral reflux by infusing contrast medium into the bladder through a urethral catheter and simultaneously monitoring the intravesical pressure. The bladder was filled and then the intravesical pressure was gradually raised to 100 cm H_2O by manual compression on the lower abdominal wall. Ureteral reflux was checked by fluoroscopy and the intravesical pressure was recorded when ureteral reflux was recognized using fluoroscopy. Excretory urography was also performed to evaluate the ureteral stricture. These postoperative examinations were performed every month over a total follow-up period of 3 months. The dogs were killed after the last evaluation and all the ureteral units were removed and examined histopathologically.

The surgery and postoperative evaluation were performed in accordance with the guidelines for care and use of experimental

animals in Jichi Medical School based on the revised NIH guide for the care and use of laboratory animals.

Results

In the type A ureteral reimplantations, eight of the ten renoureteral units showed a normal configuration of the upper urinary tract on excretory urography (Fig. 2a), and no ureteral reflux was recognized on cystography while the intravesical pressure was increased to 100 cm H_2O (Fig. 2b). In the other two renoureteral units, ureteral reflux was not recognized but severe hydronephrosis was observed at the first postoperative examination. In the resected specimens of the eight renoureteral units without hydronephrosis, a 4 Fr ureteral catheter passed smoothly through the terminal ureter covered with the de-serosalized ileal wall. Histopathological findings of the terminal ureter showed that the outside half was covered with the muscle layer and the serosa of the ileum (Fig. 3a) and the inside half was covered with the muscle layer and mucous membrane of the ileum. The ureter and periureteral tissues protruded into the ileal lumen and little inflammatory reaction was recognized in the periureteral tissues (Fig. 3b). In the resected specimens of the two renoureteral units with hydronephrosis, a 4 Fr ureteral catheter passed through the part of the ureter covered with the de-serosalized ileal wall, but it could not pass through the distal end of the ureter. A short ureteral stricture was recognized exactly at the site where the direct ureteroileostomy had been performed, though the patency of the ureter in the portion covered by the de-serosalized ileal wall was confirmed microscopically in both ureteral units.

In the type B ureteral reimplantations, four of the six renoureteral units showed grade I to II ureteral reflux at an intravesical pressure of 45 ± 30 cm H_2O, while the other two ureteral units showed no reflux. One of these two had advanced hydronephrosis and the other had no upper urinary tract dilatation. Histopathological findings showed that the structure of ureteral covering with the full-thickness ileal wall did not retain its original form in all ureteral units (Fig. 4).

In the 13 direct ureteroileostomies performed without additional antireflux procedures, ten renoureteral units showed ureteral reflux at the intravesical pressure of 15 ± 9 cm H_2O (Fig. 2b). The grade was II in four ureters and III to IV in six ureters. The other three renoureteral units had no evidence of hydronephrosis or ureteral reflux even when the intravesical pressure was as high as 100 cm H_2O. In the resected specimens of these 13 renoureteral units, a 4 Fr ureteral catheter passed through the anastomotic portion smoothly.

One dog with hydronephrosis operated by the type A method was killed 1 month after the operation to examine the cause of hydronephrosis. One other dog operated by the type A method and two dogs operated by the type B method died of causes unrelated to the surgery 2 months postoperatively. The rest of the dogs were followed-up for 3 months.

Case report

A 73-year-old-man underwent radical cystoprostatectomy with orthotopic ileal neobladder for advanced transitional cell carcinoma of the bladder on 7 November 2000. An ileal neobladder was constructed according to the technique reported by Hautmann (8). The bilateral ureteoileostomy was performed using the type A covering technique and the terminal uerter was covered with the de-serosalized muscle layer. The postoperative course was uneventful and the patient urinated urethrally without catheterization. The ureteroileal anastomotic site was evaluated radiologically. Excretory urography 1 month after the operation (Fig. 5a) and

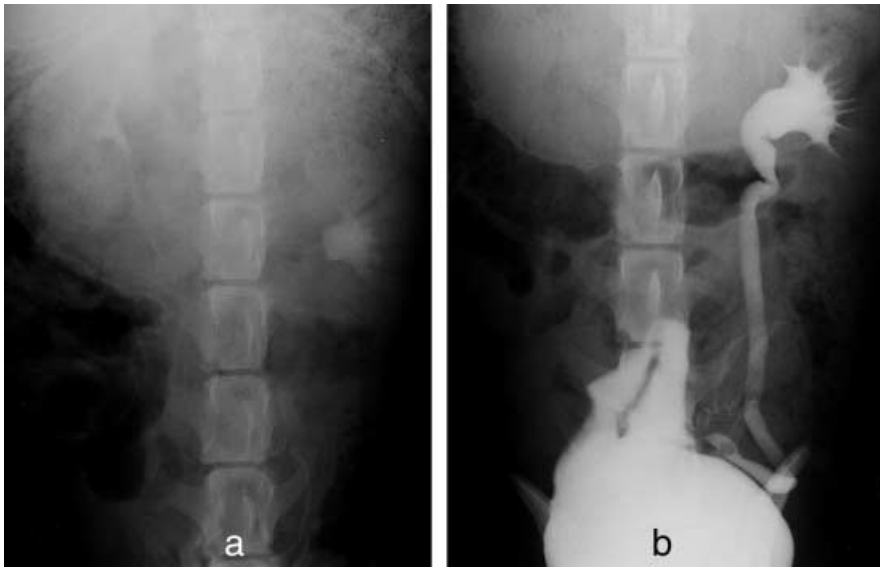

Fig. 2a, b Three month postoperative evaluation of the type A method (*right*) and direct ureteroileostomy (*left*). **a** Excretory urography shows a normal upper urinary tract *right* and a dilated urinary tract in *left*. **b** Retrograde cystography taken at an intravesical pressure of 100 cm H_2O shows no ureteral reflux *right* and grade III reflux *left*

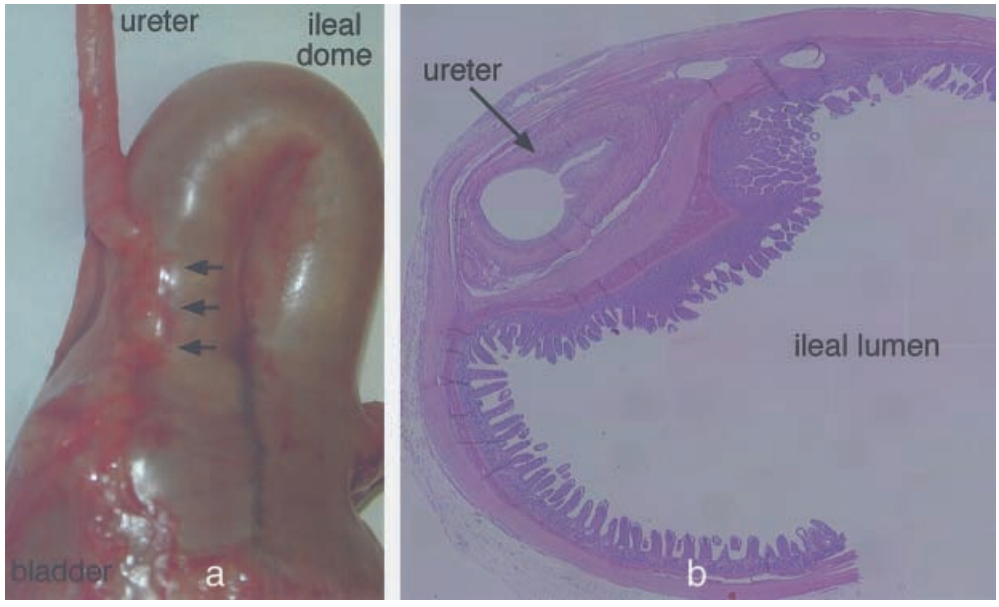

Fig. 3 **a** Macroscopic findings of the covering portion of the type A method. Terminal ureter is covered with de-serosalized ileal wall (*arrows*). **b** Microscopic findings at anastomotic site (H and E, ×10). The ureter is surrounded by a muscle layer of ileum. The ureter and peri-ureteral tissues protrud into the ileal lumen. Little inflammatory change is recognized on peri-ureteral tissues

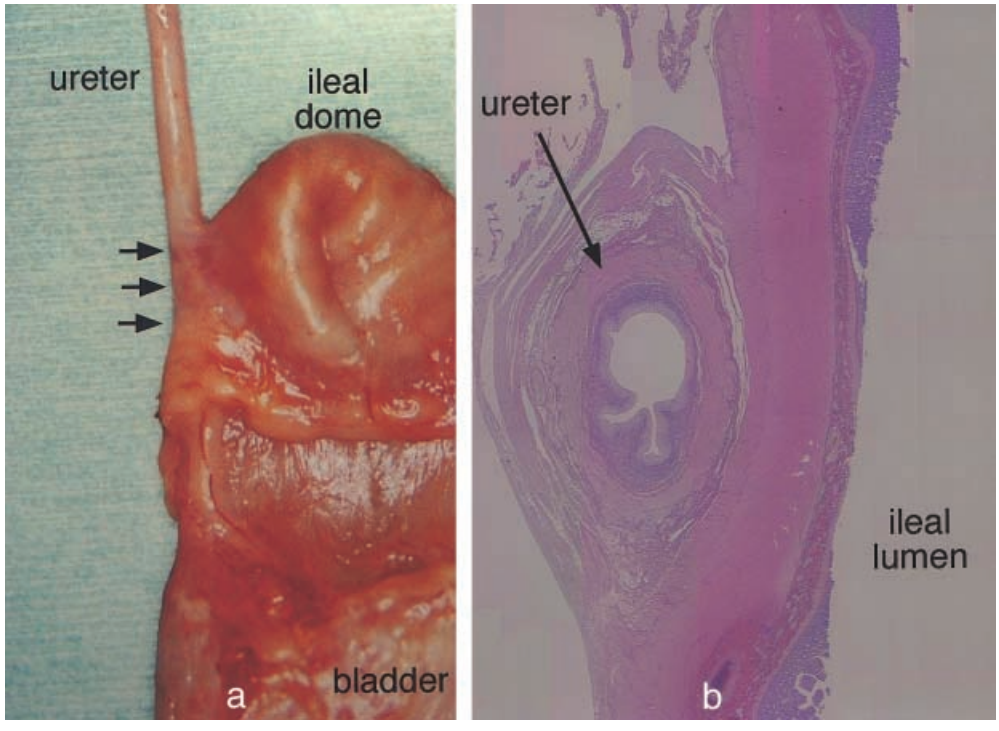

Fig. 4 **a** Macroscopic findings for the type B method. Covering portion *(arrows)* collapse. **b** Microscopic findings of at anastomotic site (H and E, ×10). Half of the outside of the ureter is not surrounded by a muscle layer of ileum. The ureter is not in the intramural part of the ileum

computed tomography 3 months after the operation showed no dilatation of the upper urinary tract. Cystography 3 months after the operation showed no reflux during either the storage phase or the voiding phase (Fig. 5b). The patient has been followed up for 5 months and no upper urinary tract dilatation or upper urinary tract infection have been recognized.

Discussion

There have been no previous reports on our technique of covering of the extraluminal terminal ureter with a de-serosalized muscle layer of the ileum for antireflux ureteroileal anastomotic procedures. The terminal ureter covered with the muscle layer and mucous membrane worked well to prevent ureteral reflux. No ureteral strictures developed when the ureter was covered with the de-serosalized ileal wall. This method can be performed from outside of the ileal pouches and the ureters can be reimplanted at any site on the ileal pouch except the connection to the mesenterium.

The procedure to remove the serosa in preparation for the ureteral covering was easy and never time-consuming. The ileal serosa was removed from the ileal wall before covering the ureter in order to soften the ileal

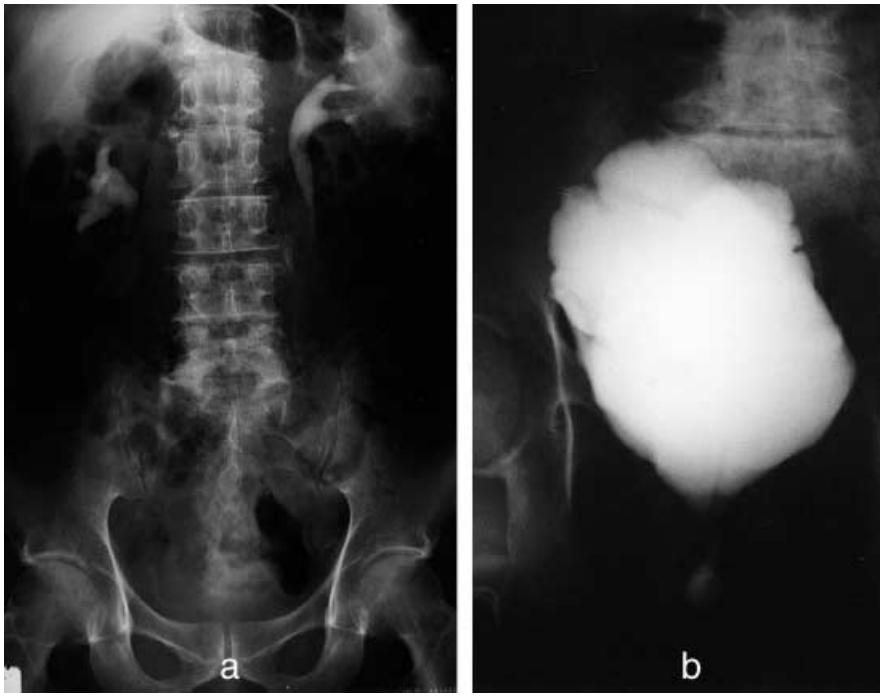

Fig. 5 **a** Excretory urography taken 1 month postoperatively shows normal upper urinary configurations. **b** Voiding cystography taken 3 months postoperatively shows no ureteral reflux

wall so that it could be wrapped loosely around the terminal ureter. During the operation, the surgeon clearly felt that the de-serosalization softened the de-serosalized part of the ileum and improved its flexibility. At autopsy, the protruding shape of the intramural ureter attested to the loose covering over the terminal ureter.

In the type A method, ureteral reflux was completely prevented until the intravesical pressure was raised to 100 cm H_2O. When the intravesical pressure was raised, the terminal ureter covered with the de-serosalized ileal wall seemed to act as a flap valve, like a submucosal tunnel. When the ileal bladders are in the storage phase, intravesical pressure is not increased while the bladder wall is extended without resistance and the flap valve mechanism will not work. Histopathological findings on the type A method showed that the terminal ureter covered with the de-serosalized ileal wall remained intramurally. This suggested that the extended ileal wall might compress the terminal ureter and work as an additional antireflux mechanism in a storage phase with a very low intravesical pressure.

The de-serosalized bared surface of the ileum provided good healing on the ureteral adventitia after the type A method, and minimal inflammatory reaction and fibrosis were recognized at the periureteral tissues. Abol-Enein et al. showed that inflammatory fibrosis of the ureteral adventitia resulted in ureteral reflux and ureteral stricture, and they also demonstrated that urine contact early after surgery caused the inflammatory change to the ureteral wall (3, 4). In the Le Duc procedure, postoperative ureteral stricture at the anastomotic site occurred some months after surgery (14). Roth et al. reported that 29 of the 142 ureters reimplanted using the Le Duc technique were obstructed, of which 15 (69%) developed 3–12 months postoperatively (17). These reports indicate that half of the ureteral strictures following the Le Duc technique occurred as late complications and that the cause of the strictures might be stiffness of the ureteral wall caused by urine contact. We propose that the de-serosalized muscle layer of the ileum facilitates a suitable healing of the reimplanted ureteral wall and prevents inflammatory fibrosis of the ureteral wall tissue.

The rate of ureteral stricture after the Le Duc ureteroileostomy was not as low as in previous reports (2, 6, 10, 13, 17, 18, 20, 21). To avoid postoperative ureteral stricture, Wenderoth et al. have applied the submucosal tunnel method for antireflux ureteroileostomy. Definitive anastomosis between the ureter and ileal mucosa was performed using this method and postoperative urine contact with the ureteral adventitia was completely eliminated. However, even after eliminating the two main causes of ureteral stricture, an 8% ureteral stricture rate was reported using this method (21).

Abol-Enein and Ghoneim reported a low rate of complications due to ureteral strictures. In this trial, a serous lined extramural tunnel method for antireflux ureteroileal anastomosis in the ileal pouch was used (2). While this technique was reported to have some merit, a W-shaped ileal sheet was needed to perform the procedure and the site for ureteroileal anastomosis was limited at the suture line on the ileal sheet. The length of the tunnelled ureters for reflux prevention was not precisely described in the report (1, 18). Since the tunneled ureter remains in the extramural part of the ileum, the antireflux function depends exclusively on the elevation of the

intravesical pressure and will not work well in a low-pressure storage phase. In our de-serosalized muscle layer covering method, the ureters can be reimplanted at any site on the reservoirs, and the method is useful in subjects with short ureters.

Although the type B method is similar to the Abol-Enein method, it could not prevent reflux. The autopsy specimens showed that the antireflux structure collapsed. The length of the ureter covered with the full-thickness ileal wall was shorter in the type B method than in the Abol-Enein method, and the ileum covering the terminal ureter was sutured on only one side in the type B method. In our study, suitable adhesion between the ureteral adventitia and the covering serosa was not obtained and the antireflux structure did not retain its original form.

In two of the ten ureteral units after the type A method, ureteral strictures occurred just at the tip of the ureter. Possible explanations for the strictures might be the difficulty in direct ureteroileal anastomosis using the thin ureters of small dogs and the early removal of the ureteral catheters by the dogs themselves. The sections of these ureters covered with the de-serosalized muscle layer did not collapse.

The theoretical benefits of reflux prevention will never be realized in practice if the ureteral reimplantation has a high rate of stricture formation. Non-antireflux direct anastomosis has been performed in humans with a lower rate of postoperative anastomotic stricture (15, 16). When the muscle layer covering method is clinically applied, the additional procedure of covering the extraluminal ureter cannot be expected to increase the incidence of postoperative ureteral stricture.

The beneficial effects of antireflux ureteral reimplantation and deterioration of the renal function under ureteral reflux were confirmed experimentally (7, 12). In our study, 46% of the 13 direct ureteroileostomies performed without the antireflux procedure showed refluxing hydronephrosis. This reconfirmed the need for reflux prevention. Three of the 13 direct ureteroileostomies showed no reflux when the intravesical pressure reached 100 cm H_2O. While it remains unclear why the reflux was prevented in these ureters, we speculated that minute scarring might have occurred at the ureteroileal anastomotic site, thereby eliminating ureteral reflux.

Our experimental studies demonstrate that the covering of the terminal ureter with de-serosalized ileal wall prevents reflux and that the burial of the ureter in the intramural space of the ileum does not cause ureteral stricture. This technique is simple and easy to perform, and only a small area of the ileum is necessary for antireflux ureteral reimplantation. We have introduced this de-serosalized muscle layer covering method (type A method) successfully in a clinical case. The type A method was easy to perform in the human subject and was not time-consuming.

We believe that this technique will be adopted as a new procedure for antireflux ureteroileostomy in ileal urinary reservoirs and will result in low incidence of postoperative ureteral strictures.

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