Review

The Urologist and the Appendix: A Review of Appendiceal Use in Genitourinary Reconstructive Surgery

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Recently, genitourinary reconstruction has experienced a renaissance. Over the past several years, there has been an expansion of the literature regarding the use of buccal mucosa for the repair of complex ureteral strictures and other pathologies. The appendix has been an available graft utilized for the repair of ureteral stricture disease and has been infrequently reported since the early 1900s. This review serves to highlight the use of the appendix for reconstruction in urology, particularly focusing on the anatomy and physiology of the appendix, historical use, and current applications, particularly in robotic upper tract reconstruction. UROLOGY 159: 10–15, 2022. © 2021 Elsevier Inc.

Over the last several decades, there has been an increase in the recognition and associated management of ureteral stricture disease. Advances in the robotic platform have optimized a minimally invasive approach for upper tract reconstruction. While the appendix is well-recognized as an option for a catheterizable channel for the bladder in children, its use for ureteral stricture disease is less well-known. In fact, unlike the buccal mucosal graft, the appendix may serve as a versatile flap for the repair of ureteral strictures in any location, though prominently on the right side. As a flap, the detubularized appendix is well-suited as an onlay patch, and in its normal luminal state, as a bypass in both proximal and distal ureteral strictures. Among the myriad of reconstructive options, the appendix has been utilized for approximately 100 years, and continues to be a viable option for genitourinary reconstruction in the appropriate clinical setting.

HISTORICAL PERSPECTIVE

Melnikoff published the first known case of ureteral substitution using appendix in 1912.[1] Wesolowski, in 1971, described the use of the appendix as a ureteral replacement in a complex patient with a solitary right kidney and a proximal stricture, with ultimate stenosis of the appendicocalycostomy, however clinical stability at 11 years.[2] In 1976, Weinberg reported a case report in which the appendix was anastomosed to the right distal ureter and bladder in the repair of a *Schistosomiasis*-related distal ureteral stricture with improved renal function and improved hydronephrosis on intravenous pyelogram noted at 8 weeks.[3] Mitrofanoff published his technique for appendiceal incorporation as a catheterizable channel in patients undergoing augmentation cystoplasty in 1980—this surgical approach remains widely in use today.[4] Malone introduced the Malone Anterograde Continence Enema procedure (appendicostomy creation) in 1990 for spina bifida patients with neurogenic bowel.[5]

Anatomy and Physiology

The vermiform appendix was first described in the 16th century by Italian surgeon Berengario da Carpi. Its precise location can be variable however is most commonly found at the posterolateral wall of the cecum with its mesoappendix including the appendicular artery coming off the terminal ileum.[6] Mean length, from a 1932 post-mortem study of 4,680 specimens, is 8.21 cm.[7] Historically considered a vestigial remnant structure, some evidence suggest that the appendix may play a role in the immune system due to the presence of significant lymphatic tissue.[6] Given this relative wealth of lymphoid tissue, and the degree of biofilm associated with commensal bacteria found in the appendix, it may serve as an anatomical reservoir and protector of healthy gut bacteria.[8] The risk of metabolic consequences and malabsorption syndromes is felt less likely with appendix in contact with urine than ileum due to lower surface area and minimal physiologic electrolyte transport.[9]

MODERN-DAY APPENDIX USE

The appendix is uniquely positioned to optimize reconstruction of the upper and lower urinary tract for

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applications including ureteral stricture disease, pyeloplasty and revision, traumatic ureteral injuries, ureteroileal anastomotic strictures, and continent catheterizable channel creation (Mitrofanoff appendicovesicostomy). Appendiceal interposition, augmented anastomotic repair, onlay, and bypass techniques have been demonstrated.

Trans-appendicular continent cystostomy (Mitrofanoff appendicovesicostomy) has been demonstrated with augmentation cystoplasty to help preserve renal function and continence in pediatric neurogenic bladder management and congenital obstructive urogenital abnormalities.[10] The Mitrofanoff channel is created using the appendix as a stoma to the dome of the bladder for clean intermittent catheterization (Fig. 1). Long-term complications include stenosis, which has been demonstrated at variable rates but seems to increase in incidence with longer-term follow-up.[10] One study of pediatric patients reported a 50% incidence of stomal stenosis at 9-month follow up. Most conduit or stomal stenosis is managed by endoscopic dilation but in up to 61% of patients in this study, revision surgery was necessary.[11] Continence rates have been documented at 100% and 79% at a mean follow-up of 3.2 years and 20 years, respectively.[12,13] Mitrofanoff creation has recently been demonstrated with both laparoscopic and robotic-assisted approaches.[14]

Appendiceal interposition is perhaps the most well-reported use of the appendix for treatment of ureteral stricture disease. Jang et al demonstrated the feasibility of an appendiceal interposition for a 6 cm proximal ureteral stricture injury sustained from blunt trauma secondary to a motorcycle accident. The pyelovesicostomy demonstrated patency at a follow-up duration of 6 months.[15] Appendiceal interposition was also utilized in a 43-year-old male who sustained penetrating trauma with a gunshot wound causing a mid-ureteral transection and associated ureteral devitalization to approximately 3 cm from the bladder.[16]

Radiation-induced ureteral stricture typically requires complex reconstruction. Lee et al, in a 2020 small case series, presented robotic-assisted laparoscopic (RAL) appendiceal bypass as effective treatment for long segment Radiation-induced ureteral stricture with success in 3/3 (100%) patients at median follow-up of 13 months (one patient was excluded for unexpected mortality on postoperative day 0).[17] Appendiceal bypass is accomplished through an anastomosis of the cecal aspect of the appendix just proximal to the known distal ureteral stricture in an end-to-side manner and the distal appendix to a cystotomy in an end-to-end fashion.[17] A later multi-institutional review of robotic ureteral reconstruction in patients with radiation-induced ureteral stricture disease demonstrated 4 of 32 patients (11.4%) who underwent appendiceal repair. Of the 34 total repaired ureteral units in this series, 30 units (88.2%) remained with radiological and clinical evidence of success at a median follow-up of 13 months.[18]

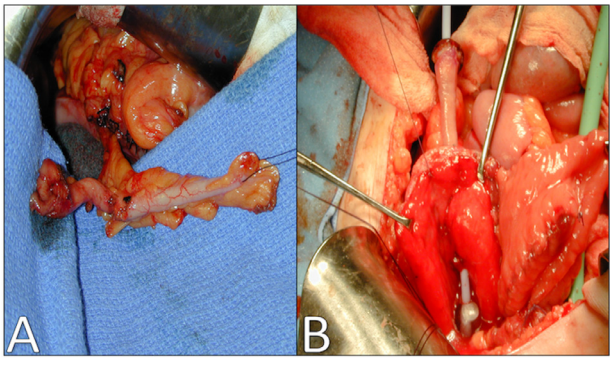

Figure 1. The Mitrofanoff continent catheterizable channel (appendicovesicostomy). (A) Appendix isolated with its associated vascular pedicle. (B) Completed appendicovesical anastomosis at the bladder dome with Foley catheter traversing the anastomosis. (Images courtesy of AAC.). (Color version available online.)

RAL interposition of the appendix has been used to successfully treat obliterative stricture due to recurrent stone disease.[19] Gn et al demonstrated the versatility of appendiceal repair in treating long segment ureteral stricture in a case report of an iatrogenic 15 cm right ureteral avulsion repaired by robotic downward nephropexy, psoas hitch, lower pole calycostomy, and 11 cm appendiceal interposition with no evidence of obstruction 6 months post-operatively.[20]

Adani et al described the utility of appendiceal interposition for the repair of an extended distal ureteral stricture, including a Lich-Gregoir ureterovesical anastomosis to the proximal ureter, following deceased donor kidney transplant. Normal allograft function including interval CT scan confirmed the appendix was an effective ureteral replacement at one-year follow-up.[21]

In contrast to utilizing the lumen of the appendix as a substitute for the ureter, an appendiceal onlay flap utilizes the detubularized appendix as a patch placed onto a longitudinally incised ureter. Such a technique may theoretically portend a lower risk of stenosis at the anastomoses of the appendix with the ureter (or with the bladder). Further, by maintaining continuity of the ureter with no dismemberment via the preservation of the ureteral plate, there may be improved maintenance of ureteral vascular supply and optimization of a water-tight anastomosis.[22-25] In 16 cases repaired with intestinal segments, Ordorica et al successfully repaired two patients with appendiceal onlay flap and demonstrated non-refluxing ureteral reimplantation with preserved renal function.[24] Wang et al previously reported a 100% success rate in nine patients with mid- (2) or proximal (7) ureteral strictures. An augmented anastomotic repair was included in this cohort.[25] In an augmented anastomotic ureteroplasty, a completely obliterated segment is excised in its entirety, the back walls of the spatulated ureter (proximal and distal to the excised segment) are re-approximated, and an onlay graft is applied to the diamond defect (Fig. 2). Laparoscopic appendiceal onlay reduces hospitalization time and post-operative pain, while also minimizing the potential morbidity of appendiceal interposition.[22, 24, 26] A multi-institutional study of 13

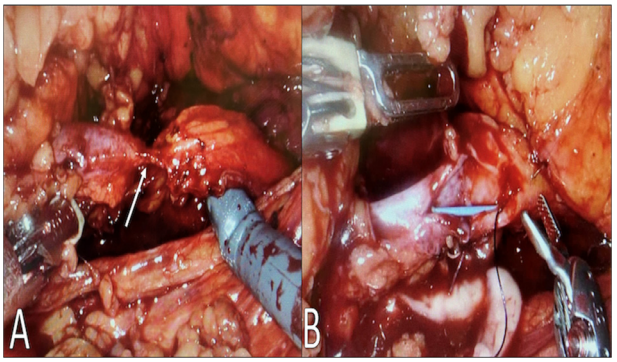

Figure 2. Augmented anastomotic ureteroplasty. (A) Completely obliterated ureteral segment has been isolated (arrow). (B) The back wall of the augmented anastomotic repair has been re-approximated following excision of the obliterated ureteral segment to prepare for placement of the appendiceal flap. (Images courtesy of SEE.). (Color version available online.)

patients, 8 undergoing RAL appendiceal onlay and 5 undergoing RAL appendiceal interposition, demonstrated an overall success rate of 92% at mean follow-up of 14.6 months.[23]

Pediatric appendiceal ureteral reconstruction has also been described. Richter et al. reported three pediatric patients that underwent replacement of the upper third of the right ureter (1) and right lower ureter (2), demonstrating no recurrent obstruction at 4, 7, and 15 years of follow-up, respectively.[27] Total and partial replacement of the ureter using the appendix and laparoscopic appendiceal interposition pyeloplasty have been demonstrated.[28,29] Cao et al presented four pediatric cases of appendiceal interposition pyeloplasty (2 right-sided, 2 left-sided) with 100% success at mean follow-up 33.8 months. Both isoperistaltic and anti-peristaltic anastomoses were utilized.[28]

Left-sided distal ureteral appendiceal interposition is feasible in adults. A contemporary retrospective series demonstrated this approach in 11 cases, three of which (27%) were performed on the left in an isoperistaltic fashion. At approximately one-year median follow-up, no patients required re-operation for stricture disease.[30] A larger series of 26 patients included 4 left-sided ureteral interpositions with a description of the steps necessary to mobilize the appendix to the left distal ureter to ensure a tension-free anastomosis, which is optimally performed robotically and through the sigmoid mesocolon. A modification in technique whereby a flap of cecum was developed along with the appendix was implemented in 22/26 cases to increase the size of the anastomotic lumen. Four patients (15.4%) experienced anastomotic stricture requiring re-intervention.[31]

RECONSTRUCTIVE CONSIDERATIONS FOR APPENDIX

There are several alternatives to appendix in reconstructive surgery, however, in ureteral strictures not amenable to primary ureteroureterostomy, the appendix is desirable given minimal morbidity associated with incorporation and high success rate.

If the appendix is unsuitable for use in the creation of a Mitrofanoff catheterizable channel a Yang-Monti (ileovesicostomy) can be undertaken. Disadvantages of the Yang-Monti include the potential for short length relative to a Mitrofanoff and the need for a small bowel resection and anastomosis, rendering it an inferior approach if the appendix is available.[32] A modification of the Yang-Monti, the so-called spiral Monti, improves length when ileum is reconstructed for the creation of a catheterizable channel.[32] Many distal ureteral strictures can be managed with a ureteral reimplantation with or without Boari flap and psoas hitch. Though useful maneuvers, these techniques may decrease bladder capacity and may be associated with reflux uropathy.[33]

For mid and proximal ureteral strictures less than 3 cm, ureteroureterostomy has traditionally been the management of choice which is technically feasible robotically with a demonstrated stricture-free rate of 94.1% in one study.[34] For ureteral strictures not amenable to a ureteroureterostomy, oral mucosa graft onlay or augmented anastomosis can be considered.[35] Disadvantages of oral mucosa graft include perioperative morbidity associated with harvest and need for omental wrap for vascular support.[36]

In patients with long or extensive ureteral strictures or defects, options include ileal ureter and renal auto-transplantation. Ileal ureter substitution harbors risk of electrolyte imbalances, mucous production, complications from intestinal anastomosis, and urolithiasis. Thus, this technique should be used in highly selective settings.[37] Kidney auto-transplantation should be performed in specialized centers with experience in transplant surgery and runs the risk of vascular complications and graft loss.[38]

SURGICAL APPROACH FOR APPENDICEAL RECONSTRUCTION

In recent years, the robotic platform has optimized the surgical approach in upper tract reconstruction in that it affords improved visibility, decreased morbidity, and expedited convalescence relative to open surgery.

Preoperative Considerations

Certain medical conditions, prior appendectomy or appendiceal operation, adhesive disease, and congenital absence will prevent appendiceal use. Cross-sectional imaging should be reviewed to approximate the location and length of both the stricture of interest and appendix. Concomitant anterograde and retrograde pyelograms ("up-and-down-o-gram") should be performed ahead of surgery. Recently, work by Lee et al has demonstrated that ureteral rest, which is defined as absence of ureteral stent or percutaneous nephroureteral stent for ≥4 weeks, prior to robotic ureteral reconstruction improved success rates,

reduced blood loss, and decreased use of buccal mucosal graft.[39] Though this study did not directly evaluate the implications of ureteral rest for ureteral reconstruction with appendix, the principle likely remains applicable in this setting to allow for a more mobile and easily manipulated ureter.

Our bowel preparation of choice is two bisacodyl tablets the day prior to surgery. Parenteral antibiotics should be administered 30-60 minutes prior to incision. As most patients with ureteral stricture disease have had prior urinary tract infections, it is critical for antibiotic selection to be effective against historical bacteria, particularly in those with a ureteral stent or nephrostomy tube.

Open Surgery

We support selective reservation of an open approach to the rare case where robotic progress is not possible requiring conversion to open or based on surgeon experience and preference. Open ureteral reconstruction using appendix has been described for various indications including proximal ureteral stricture disease, distal urothelial cancer, and ureteral necrosis after kidney transplantation.[15,21,28,40,41]

Location of the stricture of interest will dictate if maneuvers such as Psoas hitch, Boari flap, or downward nephropexy are required to ensure a tension-free anastomosis. Smaller case series have demonstrated that appendix use for open ureteroplasty is technically feasible with favorable outcomes.[27,29,40,42,43] The incision utilized, typically a midline laparotomy, should allow for access of the entire ureter and appendix. However, a robotic approach should be strongly considered given that a large incision is not necessary for specimen extraction and exposure of the entire ureter and appendix is necessary.

Minimally-Invasive Surgery (MIS)

Laparoscopic and robotic-assisted surgery afford improved visibility, intracorporeal maneuverability, and expedited convalescence.[44,45] Lithotomy positioning is not always necessary and most patients can be positioned supine. Laparoscopic ureteroplasty using appendiceal onlay was first described by Reggio et al.[26] Several studies have since demonstrated the technical feasibility and decreased morbidity of appendiceal use via MIS.[17,19,20,24] Indocyanine green (ICG), visualized with near-infrared fluorescence (NIRF), can be injected via nephrostomy tube or ureteral catheter to identify structures of interest or administered parenterally.[46] One particular disadvantage of intra-ureteral ICG use is that upon ureteral transection, ICG spills into the surgical field and generally prohibits any further application. We favor avoiding the intra-ureteral use of ICG except for cases in which identification of the ureter is not technically feasible otherwise. Instead, Firefly Fluorescence Imaging/NIRF is used to view the white light of the ureteroscope as it transilluminates the ureter. Reserving ICG for intravenous use allows for an optimized assessment of the vascular variability of the ureter and the appendix.

The da Vinci Xi (Intuitive Surgical, Inc.) platform allows for ICG, TilePro, and facile port placement with side docking to allow for intraoperative access to the urethra—all of which are beneficial adjuncts for localizing the repair and assessing the viability of the appendiceal flap. The da Vinci Single Port robotic platform, with its decreased port burden, may allow for more facile access to the urethra in patients in the lateral decubitus position, however one relative disadvantage is current inability to use Firefly NIRF, thus ICG cannot be leveraged in this setting.

Our Technique

For distal ureteral strictures, a dorsal lithotomy position with a table tilt to the contralateral (typically to the left) is feasible. The ports should be placed slightly cephalad to the umbilicus to allow for access to the ureter superior to the common iliac vessels. Further, the ports can be shifted slightly cephalad on the ipsilateral side (typically the right) and shifted slightly caudal on the contralateral side. A left-sided 12 mm assistant port will allow for facile access and to permit insertion of a laparoscopic stapler.

For proximal or pan-ureteral strictures, the patient should be placed in the lateral decubitus position with the genitals prepped onto the field in male patients or on a split-leg table with table tilt towards the contralateral side in female patients. Concurrent ureteroscopy with TilePro permits visualization of the endoluminal ureter while Firefly visualization can highlight the transilluminated white light from the ureteroscope from the robotic view. In this way the precise location of the ureteral stricture is identified from within the ureter. Passage of the ureteroscope after incision or excision of the stricture of interest verifies no additional ureteral strictures. Passage of a ureteroscope after completing the repair ensures the ureteroplasty is widely patent and water-tight.

After identifying the ureteral stricture of interest, it is incised longitudinally and measured. If a completely obliterated segment is noted, in which no urothelium would be identified upon incision, the segment is excised in its entirety and an augmented anastomotic repair is pursued. Often, mobilization of the ureter proximally and distally, as well as downward nephropexy, may be necessary maneuvers to optimize an anastomosis off tension. The cecum and ascending colon are next mobilized sufficiently to permit the appendix to reach the ureteral stricture. We have found that for proximal ureteral strictures, the appendix is typically placed in the iso-peristaltic orientation, that is, the tip is rotated towards the ureteropelvic junction. For mid and distal ureteral strictures, we find that leaving the appendix in the anti-peristaltic orientation (ie, tip towards the bladder) seems to optimize the positioning of the closure. Essentially, the tip is the most mobile aspect of the appendix and should be directed towards the furthest part of the stricture. The appendix is next circumferentially dissected at its insertion into the cecum. A window into the meso-appendix is created and a 12 mm Endo-GIA stapler with a bowel load is utilized to

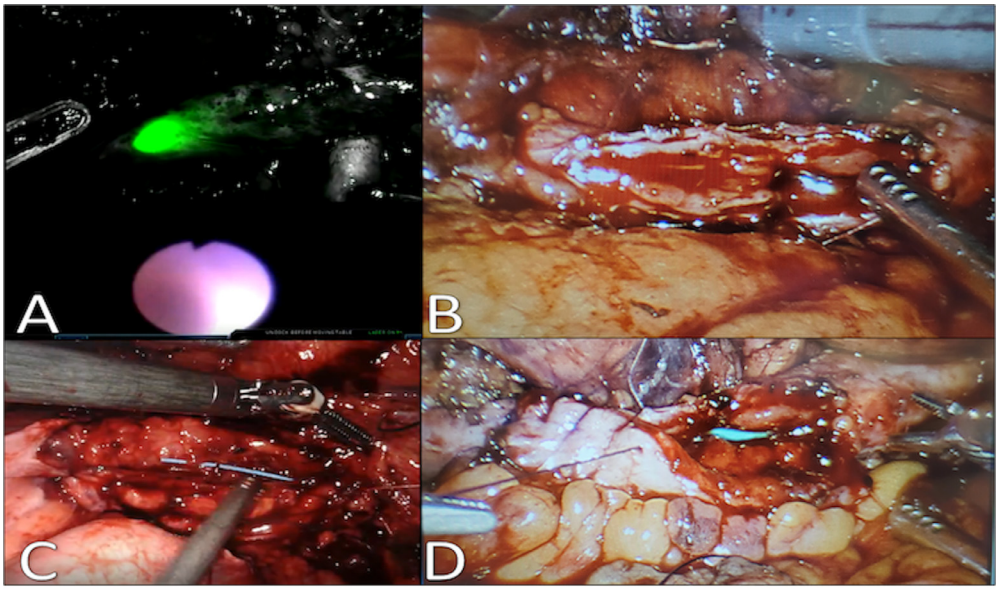

Figure 3. Robotic ureteroplasty with appendiceal onlay. (A) Identification of the stricture of interest with simultaneous ureteroscopy and robotic visualization using TilePro and Firefly technology. (B) Detubularization of the appendix after isolation from the cecum. (C) Aligning the appendix along the side of the intended onlay anastomosis. (D) Suturing of the appendiceal onlay flap into position. (Images courtesy of SEE.). (Color version available online.)

staple-ligate the appendix at its insertion into the cecum. If an appendiceal interposition is planned, the two tips are excised, the appendix is cleaned of its feculent contents, the cephalad and caudal ends are spatulated appropriately, and anastomosis follows. If an appendiceal onlay is planned, the appendix is detubularized and oriented alongside the ureteral stricture. Intravenous ICG is next administered and the vascular variability of the ureter and appendix are assessed. Devascularized portions of the appendix are excised. The near edge of the appendix is anastomosed to the near edge of the detubularized ureteral segment. The far edges of the appendix and ureter are next anastomosed. We typically use 4-0 Vicryl suture in an interrupted fashion to approximate appendiceal mucosa to ureteral mucosa (Fig. 3). Ureteroscopy is performed to ensure the repair is widely patent and watertight. A ureteral stent is then placed and confirmed to be appropriately positioned with an abdominal X-ray at the conclusion of the case.

Patients are maintained on prophylactic antibiotics for the duration of the ureteral stent, which is removed in the outpatients setting in approximately four weeks. A renal/bladder ultrasound and nuclear medicine Lasix renogram are performed 6-8 weeks later to document function of the kidney and unobstructed drainage.

CONCLUSION

The appendix is uniquely positioned and well-suited for incorporation in both upper and lower urinary tract. Its utility in the genitourinary system is favorable for a variety of reconstructive applications.

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