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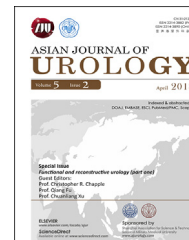
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Review

# Adult iatrogenic ureteral injury and stricture—incidence and treatment strategies

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**Abstract** Iatrogenic ureteral injuries and strictures are relatively common complication of pelvic surgery and radiation treatment. Left untreated they are associated with severe short- and long-term complications such as urinoma, septic state, renal failure, and loss of a renal unit. Treatment depends on timing of diagnosis, as well as extent of injury, and ranges from simple endoscopic management to complex surgical reconstruction under usage of pedicled grafts. While recent advances in ureteral tissue engineering are promising the topic is still underreported. Historically a domain of open surgery, laparoscopic and robotic-assisted approaches have proven their feasibility in small case series, and are increasingly being utilized as means of reconstructive surgery. This review aims to give an outline of incidence and treatment of ureteral injuries and strictures in light of the latest advances.

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## 1. Introduction

Iatrogenic injuries and radiation treatment cause 75% of all ureteral strictures [1], which represent a rare but challenging field of reconstructive urology [2]. If left untreated they can result in serious short- and long-term complications such as urinoma and abscess formation, septic state,

development of fistula, chronic renal failure, and even lost of a renal unit [3].

The management of ureteric injuries and strictures shows a broad range of therapeutic options from endoscopic management to complex reconstruction or even renal autotransplantation, and depends on the location, i.e., proximal, mid, or distal ureter and the length and severity

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of the injury [4,5]. While the distal third of the ureter is a frequent site of injury (91%), the middle and proximal third are rarely affected (7% and 2%, respectively) [4,6].

Due to its retroperitoneal location, mobility, and diameter as well as peritoneal coverage the ureter is shielded from external and blunt trauma. At the same time the ureter shows great proximity to anatomic structures that are common sites of gynecologic and general surgery, such as gonadal and uterine vessels, the cervix, iliac arteries, inferior mesenteric, and sigmoid vessels as well as colon and rectum [7]. Further it has a delicate subadventitial blood supply that is segmentally provided by the renal, gonadal, common iliac artery, and the aorta. Taken together its unique anatomy and proximity to other pelvic and abdominal organs render it prone to iatrogenic trauma. Common mechanisms of injury include either direct trauma (transection, suture ligation, crush injury, and coagulation), or indirect trauma that is afflicted by relative ischemia due to large caliber instruments, devascularization, and thermal injury [2,8–10].

This review aims to give an outline of incidence rates, diagnostics, and treatment for ureteric injuries and strictures.

## 2. Incidence

Gynecologic procedures account for the majority of ureteral injuries with 64%–82%, while colorectal, vascular pelvic, and urologic surgery account for approximately 15%–26% and 11%–30%, respectively [7,10,11].

Incidences of ureteral trauma in gynecologic surgery have been reported to range between 0.3%–2.5% [12–17] for hysterectomies and standard pelvic operations, and <5% of oncological procedures such as radical hysterectomy [4]. In an extensive review of 3344 articles the leading cause of ureteral injury in laparoscopically assisted surgery was vaginal hysterectomy (20%), followed by excision and resection of endometriosis (12.8%), oophorectomy (11.4%), pelvic lymphadenectomy (10%), sterilization (7.1%), and either adhesiolysis, lymphocele drainage, or electrocoagulation (4.3%) [18].

Of note, under the advent of minimally invasive surgery an increase of ureteral injuries in gynecological and general surgery has been seen in some [10,19,20] but not all conducted studies [21,22]. A prospective multicenter study that assessed laparoscopic hysterectomies over nearly 2 years found drastic differences in incidences of 13.9 and 0.4 cases per 1000 procedures in laparoscopic and open hysterectomy, respectively [13]. Another work, focusing on laparoscopic colectomy corroborated significant differences in incidences of 0.66% and 0.15% in laparoscopic and open cases, respectively [20].

In regard to general surgery the commonest causes for ureteral injuries are low anterior and abdominal perineal resection, and incidences between 0.24% and 5.70% have been reported [11,19–21].

Urologic interventions including ureteroscopy, lymphadenectomy, and urinary diversion account for up to 13% or ureteral injury and strictures. Most commonly they are attributed to endoscopic procedures that involve stone treatment [1,7]. Mucosal abrasion occurs in 0.3%–4.1%, perforation occurs in 0.2%–6.0%, and ureteral avulsion amounts to 0.3%–1.0% of ureteroscopy. The formation of

ureteral stricture as a consequence was seen in 0.5%–2.5% of cases [5,11,23–26].

Strictures associated with radiation treatment usually become apparent with a latency of several years and depend on the treatment modality and delivered dose of radiation. Previous studies reported incidence rates of 1.8%–2.7%, and 1.2% at 10 years of follow-up in prostate cancer and cervical cancer, patients, respectively [27].

## 3. Diagnosis and initial treatment

The treatment of ureteric injuries and strictures depends on their location, extend, and time of discovery. Ideally they are treated and repaired at the time they originate; otherwise therapeutic mainstay is to restore urinary drainage in order to prevent complications such as secondary retroperitoneal fibrosis, sepsis, and renal failure [1,3].

The majority of injuries (>65%) are diagnosed post-operatively [5,18]. A retrograde pyelogram is the diagnostic tool of choice, despite its high sensitivity it allows for placement of an indwelling stent that restores urinary drainage. If a retrograde pyelogram is not available, a computed tomography with intravenous urography (CT-IVU) should be performed and a percutaneous nephrostomy placed in combination with an attempt to place an indwelling stent in antegrade fashion. In short defects ( $\leq 2.5$  cm) the placement of an indwelling stent, placed either retro- or antegradely makes for an adequate treatment and is removed after 2–6 weeks [6,28,29]. Injuries associated with ureteroscopy are only rarely treated with open surgery (0.22%) [25]. Smaller case series have even demonstrated satisfactory results after endoscopically realigning completely transected ureters. Studies were limited by short-term follow-up of 21.5 and 26.5 months and small cohort size but nevertheless success rates of 75% (6/8) and 78% (14/18) were reported, respectively [30,31].

Traditionally a waiting period of 6 weeks to 3 months had been suggested for secondary reconstructive surgery to take place. This was suggested in order for inflammation, fibrosis, adhesions, tissue edema and distorted anatomy to subside [6,32]. Selected other authors, however, have reported equal outcome for immediate reconstruction after diagnosis compared to deferred repair [33,34]. Taken together, these results do not allow for a final conclusion and timing of ureteral repair should be decided on an individual base and at the discretion of the surgeon.

## 4. Open reconstructive approaches

Endoscopic management holds its place in the treatment of minor injuries and management of strictures in patients unsuitable for surgery. However in regard of ureteral strictures, the long-term success rates of endoscopic management (stenting, dilation, endoureterotomy) are limited [2] and surgical management should be undertaken.

Ureteral reconstruction, regardless of the surgical approach follows basic principles: Debridement of necrotic tissue, spatulation or ureteral ends, tension free and watertight mucosa-to-mucosa anastomosis with absorbable sutures, internal stenting and external drain [35].

The surgical approach, *vide supra*, depends on location and extent of the stricture. Ureteral transections or short strictures (2–3 cm) can be repaired by ureteroureterostomy. This is mostly the case for intraoperative consults, where a ureter has been transected. While this approach has the advantage of preserving the natural anti-reflux mechanism of the bladder, it has, however, not gained broad acceptance, as it is associated with higher rates of complications including fistula formation, necrosis, and (re-) stricture [36].

The majority of strictures are seen in the distal third of the ureter, below the pelvic brim and can be repaired with ureteroneocystostomy. A non-refluxing technique is the preferred approach and clinical consensus as it minimizes vesico-urethral reflux, risk of infection and secondary renal insufficiency [5,28]. Among the many proposed techniques, those described by Lich-Gregoir [37,38] and Politano-Leadbetter [39,40] have gained greater popularity. Reflux protection is achieved by either extra- or trans-vesically creating a submucosal tunnel (usually three to four times the diameter of the ureter) through which the ureter is implanted [37,38,40]. Notably a previous retrospective study was not able to determine a difference between refluxing and non-refluxing implantation in adults [41].

In the majority of cases, however, a ureteroneocystostomy is combined with a psoas hitch maneuver [42] or a Boari flap [43,44] in order to cover a greater distance and allow for tension free anastomosis. For a psoas hitch (covering 6–10 cm of defect) the detrusor muscle is attached to the psoas muscle tendon and the ureter reimplanted as described above. Caution must be placed not to injure the genitofemoral nerve, which crosses the psoas muscle. If further length has to be covered for example in mid-ureteral defects, or the distal blood supply of the ureter is questionable, a Boari tubularized bladder flap solely or in combination with a psoas hitch can be utilized (covering 12–15 cm). Here the bladder is anteriorly incised, a flap turned cranially is then tubularized and the ureter reimplanted in non-refluxing fashion. In order to avoid flap ischemia, a length to width ratio of 3:2 should not be exceeded. Both techniques showed promising long-term results reaching up to 97% success rates at 4.5 years of follow-up [34].

Only in rare cases, such as previous radiation treatment, Crohn's disease, and other conditions that preclude bowel interposition, do ureteral injuries or strictures show an extent or clinical context that would require reconstruction in form of transureteroureterostomy or even renal autotransplantation.

Transureteroureterostomy is realized by mobilizing the donor ureter, passing it through the posterior peritoneum anteriorly to the bifurcation of the vessels, and to the contralateral site where it is anastomosed to the recipient ureter. In a series of 63 cases, notwithstanding at a reconstructive center, short-term complications of 23.8% were reported, while long-term success was attained in 96.4% [45].

Renal autotransplantation involves harvesting the kidney and creating an anastomosis with the iliac vessels and bladder [46].

Both treatment options are considered ultimate reserves and are rarely performed as they demonstrate a high rate of short-term complications and entail significant risks such

as injury to the contralateral ureter and kidney and even renal loss [2,5,45].

At rare occasions the length and complexity of a stricture, or a poor bladder condition preclude reconstruction with use of urothelial tissue. In these cases segments of bowel can be used as a substitute instead. To date several gastrointestinal segments have been proposed, such as appendix, stomach, and colon, yet ileum has become the most frequently used source. The technique was first described in the 1901 for the treatment of tubercular stenosis, popularized in the late 1950s and has since become a valuable treatment option with acceptable long-term outcomes [47,48]. The technique involves replacement of the ureter with a tubularized, pedicled segment of ileum measuring 15–20 cm, which is anastomosed in isoperistaltic fashion in order to avoid functional obstruction. In case of an extensive bilateral ureteric stricture the ileal segment can even replace both ureters [48]. Long-term complications of ileal substitutes include recurring infections, prolonged mucus formation and obstruction, hyperchloraemic metabolic acidosis, and stricture. Further there is a low incidence of secondary malignancies in ileal ureters of 0.8% at a mean of 20.2 years (standard deviation  $\pm$  10.9 years) of follow-up [49]. Nevertheless this procedure offers long-term success rates of >80% and has proven a viable treatment option [48,50].

As the graft elongates and dilates over time, side effects such as mucus built-up and metabolic complications are likely to progress [51]. This has led to several modifications of the procedure including tailoring of the ileal segment in order to reduce the mucus producing and absorbing surface of the graft [52]. Such principle is followed by the Yang-Monti procedure, which further subdivides an ileal segment into 2–3 parts. These are then longitudinally incised under preservation of the mesenterial blood supply, which results in formation of three rectangular strips whose length corresponds to the circumference of the ileum [53,54]. They are joined longitudinally and tubularized, thereby forming the ureteral substitute, which now can be reimplanted in a non-refluxing fashion [55]. In patients unfit for an ileal substitute, either after radiation treatment of the pelvic region or due to complex adhesions, the Yang-Monti procedure can instead be performed with a colonic segment. Both approaches, colonic and ileal substitutes, have been evaluated with long-term follow-up of up to 54 months and shown success rates of 71.4% [51,56–58].

## 5. Ureteral grafts, tissue engineering

Numerous grafts have been evaluated for ureteral substitution including free autologous (buccal mucosal, and vein), synthetic and non-synthetic (Gore-Tex, small intestinal submucosa (SIS)), and pedicled grafts (stomach, appendix, colon, ileum). These attempts were complicated by the toxic effect of urine and delicate anatomy of the ureter and have led to the prevalence of pedicled bowel segments [2,51]. Reports on the use of buccal mucosa transplants, a technique success fully used for urethral reconstruction [59], are scant and rely on small series with short-term follow-up [60,61]. A recent publication reported a 100% success rate with a median follow-up of 15.5 months applying buccal mucosa transplants in robotic assisted ureteral reconstruction. The authors used

an onlay technique with an omental wrap to cover strictures of 2–6 cm in four patients [61].

The literature on tissue engineering for ureteral substitutes is scarce and limited to experimental studies [62]. Earlier studies relied on acellular scaffolds such as SIS, collagen, or Gore-Tex, that were implanted in animal models in order to lead to regeneration of smooth muscle and urothelial cells [63]. The observed high rates of fibrosis were likely due to a lack of functional urothelium and adequate vascularization [62]. This has led later studies to incorporate cell seeding of acellular scaffolds prior to implantation. Different cell types have been explored, such as primary smooth muscle or urothelial cells, mesenchymal or adipose-derived stem cells. Optionally pre-implantation of scaffolds was used in order to facilitate urothelial regeneration [62–66]. Notwithstanding encouraging advancements, the current state of research in ureteral tissue engineering is scant and future efforts should attempt to identify cell sources, scaffolds, and implantation techniques that can be tested in preclinical animal models [62].

## 6. Minimally invasive reconstruction

Open surgery remains the mainstay of complex ureteral reconstruction. Laparoscopic and robotic assisted approaches, however, are constantly refined, and expanded to different indications [67]. While minimally invasive approaches are limited in textile feedback and show longer operative time, they have been shown to result in reduced blood loss, and shorter length of stay [68]. Notably with the widespread adoption of robotic platforms laparoscopic approaches are increasingly replaced [69].

Current comparative studies and outcome reports rely on small series and a certain selection bias has to be considered interpreting them. The first laparoscopic ureteroureterostomy was described in 1992 [69]. Since then, ureteroureterostomy has remained the most commonly reported procedure in laparoscopic and robotic surgery alike with success rates reaching >90% [67,70]. Comparative studies have also demonstrated equal success with greater operative time (253 min vs. 220 min), reduced blood loss (86 mL vs. 258 mL estimated blood loss), and shorter length of stay (3 days vs. 5 days) for the Boari-flap [71].

Reports on transuretero-ureterostomy, and ileal-interposition to date rely on case reports that do not allow for further conclusions [72,73].

## 7. Conclusion

Ureteral injuries and strictures are mostly caused iatrogenic and in the majority affect the distal third of the ureter. Treatment depends on extent, cause, and timing of diagnosis, and repair of injuries is ideally delivered at the time of incidence. Restoring urinary drainage is paramount and most minor injuries can be treated endoscopically with an indwelling stent.

Distal strictures can be managed with ureteroneocystostomy if necessary in combination with a psoas hitch. Mid- and proximal strictures can be managed with ureteroureterostomy or a Boari-flap. Only rarely are transureteroureterostomy, renal autotransplantation

or an ileal substitute being employed. While ureteral reconstruction remains a domain of open surgery laparoscopic and robotic assisted approaches are increasingly adopted with encouraging results.

## Conflicts of interest

The authors declare no conflict of interest.

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