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Vesicourethral Anastomotic Stenosis after Prostate Cancer Treatment

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Abstract

Purpose of Review To describe the epidemiology, pathogenesis, and management of vesicourethral anastomotic stenosis after prostate cancer treatment.

Recent Findings Injectable scar modulating agents administered at the time of direct visual internal urethrotomy of vesicourethral anastomotic stenoses have been shown to improve endoscopic treatment outcomes. Trials are ongoing to find the optimal agent and delivery system. Novel tissue engineering techniques are in development and hold promise.

Summary Vesicourethral anastomotic stenosis after the treatment of prostate cancer is a challenging complication for patients and urologists. Stenoses are prone to recurrence after endourologic treatment. Open repair is technically demanding and carries substantial patient morbidity. The need for adjuvant or salvage radiation therapy after radical prostatectomy worsens outcomes of both endourologic and formal repairs. Postoperative worsening of urinary incontinence is common after vesicourethral anastomotic stenosis repair and can ultimately require placement of an artificial urinary sphincter or male sling. Occasionally urinary diversion, indwelling foley catheter, or clean intermittent catheterization is necessary when reconstructive options have been exhausted. Adjunctive measures to improve endourologic management such as hyperbaric oxygen and transurethral injection of anti-fibrotic agents have been an area of interest in recent years and show promise.

Keywords Vesicourethral anastomotic stenosis · Bladder neck contracture · Prostatectomy · Direct visual internal urethrotomy · Mitomycin c · Hyperbaric oxygen

Introduction

Vesicourethral anastomotic stenoses (VUAS) after the treatment of prostate cancer can be a morbid complication for patients and a challenge for urologists. VUAS as result of prostatectomy should be distinguished from the broader definition of bladder neck contractures (BNC) which can refer to either VUAS or stricture after transurethral interventions when the prostate remains in situ. Patients with VUAS can variably present with urinary incontinence, weak stream, urinary retention, lower urinary tract symptoms and recurrent urinary tract infections [1]. Management is complicated by frequent recurrence after endoscopic treatment attempts and substantial technical demands for definitive reconstruction [2••]. The need for multimodal treatment of a patient's prostate cancer with radiation further exacerbates the complexity of management [3, 4]. When reconstructive options have been exhausted, urinary diversion, self-dilation, or long-term indwelling catheter is occasionally necessary.

Estimates of the incidence of VUAS after radical prostatectomy range from 1.6% to 11.1% in contemporary series. The incidence has decreased with the migration from an open retropubic approach to the robotic assisted laparoscopic technique [5–12]. Though incompletely described, an etiology implicating vascular compromise can be inferred from retrospective series which note a higher incidence in patients with advanced age, morbid obesity, renal insufficiency, coronary

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artery disease and active smoking. Other factors variably implicated include vesicourethral anastomotic urine leaks and pelvic hematomas [7, 8, 11–13].

Initial management of VUAS is classically with dilation or direct visual internal urethrotomy (DVIU). The success rate for first-time endoscopic management is quoted as 44% in a large retrospective contemporary series. Subsequent success rates for second- and third-time endoscopic procedures decrease precipitously [2••]. A history of adjuvant or salvage external beam radiation therapy (XRT) portends a worse prognosis. Given these modest results there has been interest in improving outcomes with hyperbaric oxygen (HBO) treatments and injection of scar modulating agents [3, 4, 14–18].

The small vessel endarteritis caused by radiation treatment can be partially ameliorated by serial treatments with pressurized oxygen. The evidence for utility is primarily in radiation cystitis and currently only holds a theoretical benefit in VUAS [17, 18]. The agents which have received the most attention for transurethral injection are Mitomycin C (MMC), an anti-fibrinogenic deoxyribonucleic acid (DNA) alkylating agent, and triamcinolone. Though the quality of evidence is suboptimal, there is some indication that injection of MMC can be a useful adjunctive maneuver [14–16, 19, 20].

Failure of definitive endoscopic management requires either serial self-dilation, long-term indwelling urethral catheter, formal repair or urinary diversion. The decision to attempt VUAS reconstruction is dependent on the patient's health, inclination to undergo further surgery after prostatectomy, and the treating urologist's perception of urethral salvageability. Initial approaches for definitive repair primarily describe a combined abdominal and perineal approach with creation of a new vesicourethral anastomosis. More recent approaches include transvesical robotic assisted approaches with buccal mucosa graft (BMG) inlay or local tissue advancement flaps [21, 22]. Correcting the VUAS can worsen incontinence and patients should be advised they may require subsequent artificial urinary sphincter (AUS) or male sling for continent voiding [23].

There is abundant room for improvement in the management of VUAS. Large knowledge gaps exist in the pathogenesis of VUAS formation and scar tissue formation in general. Targeting specific fibrosis pathways with either injectable or transurethrally absorbed medications hold promise. Efforts at tissue engineering a suitable graft for urethral strictures and VUASs are ongoing.

Epidemiology

A study from a prostate cancer disease specific registry of over 3000 men from 1995 to 2006 found an 8.4% stricture rate in non-irradiated patients after radical prostatectomy. They did not distinguish between open and robotic assisted laparoscopic techniques [6]. A slightly more recent study of 8837 patients from 2003 to 2007 in the Surveillance, Epidemiology, and End Results (SEER) database distinguished the minimally invasive approach from the open retropubic prostatectomy; there were significantly more VUASs in the open versus minimally invasive approach (14.0% vs 5.8%) [5].

Observational series have also shown a trend toward decreased VUAS formation for laparoscopic postatectomies though high-volume open surgeons have also had excellent results. In 753 patients that underwent open retropubic radical prostatectomy (RRP) there was a 4.8% rate of VUAS. In a second larger series of 4132 RRPs, a 2.5% rate of VUAS was identified. Comparatively, in a series of 930 patients treated with robotic assisted laparoscopic prostatectomy (RALP) there was only a 1.4% rate of VUAS. A retrospective review of 100 consecutive open prostatectomies and 100 robotic assisted procedures performed by a single surgeon noted no VUAS in the robotic series versus 9% in the open radical prostatectomy group. This was corroborated more convincingly in retrospective review of 988 patients in which 695 patients underwent open surgery and 293 patients underwent RALP. The study noted a 1.4% risk of VUAS in the RALP group versus 2.6% in the RRP group [9–13] (Table 1).

Risk Factors and Pathogenesis

Mechanistic in vitro and in vivo studies are lacking to describe the pathogenesis of VUAS. Microvascular disease has been implicated in anastomotic complications in multiple disease processes. In a series of 467 open radical prostatectomies, comorbidities known to cause microvascular disease including diabetes mellitus, hypertension, coronary artery disease, and active smoking were associated with a higher rate of VUAS. Similarly, age, renal insufficiency, and morbid obesity were also predictive of VUAS formation in a combined series 4592 laparoscopic and open radical prostatectomies [7, 8].

It has been suggested that the robotic anastomosis, in which meticulous mucosa to mucosa apposition is created, is protective over the standard interrupted tennis racket closure commonly used in open retropubic radical prostatectomy [13]. Technical factors, other than a minimally invasive versus open approach, associated with an increased risk of VUAS formation include anastomotic leak, increased intraoperative bleeding, and pelvic hematoma. This may be an overlapping spectrum given pelvic hematomas can displace and distract healing anastomoses causing a urine leak. Migrating foreign bodies such as staple lines from division of the dorsal venous complex (DVC) and hemostatic clips have also been implicated in the formation of VUAS [8, 10].

A substantial risk of VUAS is seen in patients treated with adjuvant or salvage radiation therapy. The normal time course for development of VUAS is also extended. In general,

Table 1 Incidence of VUAS in contemporary prostatectomy series by surgical approach

Series	Year	Technique	Patients (n)	Incidence (%)
Borboroglu & Amling	2000	RRP	467	11.1
Park & Lepor	2001	RRP	753	4.8
Erickson & Catalona	2009	RRP	4132	2.5
Elliott & Carroll	2009	RRP/RALP	3310	8.4
Sandhu & Rabbani	2010	RRP/RALP	988	2.2
Breyer & Carroll	2011	RRP/Laparoscopic	3458	4.3
Parihar & Kim	2014	RALP	930	1.6

VUASs after radical prostatectomy without radiation present in the first 6 months. In a prospectively evaluated cohort of 705 consecutive prostatectomies the median time to VUAS occurrence was 3.8 months [24]. Salvage or adjuvant radiation associated VUASs can present years after the delivered therapy. Salvage prostatectomy after primary radiation treatment of prostate cancer also increases the risk of VUAS [3, 4, 12].

Surgical Management of Vesicourethral Anastomotic Stenosis

Endourological Management

Direct visual internal urethrotomy (DVIU) and urethral dilation have been the traditional first line endourologic management of VUASs for decades. Initial descriptions of DVIU primarily described cold-knife incision in a single location. More recent publications describe multiple (tri or quadrant) incisions with either a cold knife or laser, balloon dilation, balloon dilation with incision or transurethral resection of the contracture. There are currently no urethral stents approved for the urethral strictures in the United States although there are stents available internationally (e.g., Memokath stent). Success rates of endoscopic treatment modalities without the use of adjunctive anti-fibrotic agents are summarized in Table 2. The lack of prospective studies, heterogeneity of inclusion criteria, and a publication bias for cohorts treated by experts that see mostly refractory cases make an accurate estimation of the efficacy of endoscopic management difficult to determine.

The success rates in the small series of novel treatments can be promising but when not evaluated by prospective well-powered studies the results should be incorporated into clinical practice cautiously. A large retrospective review of 142 patients managed by a variety of techniques, with rigorous inclusion criteria and follow-up, likely gives a relatively realistic description of expected success rates of endoscopic management. The combined result of laser incision, urethral dilation, cold knife incision, and stent placement lead to a 44% success rate after a single procedure. Laser incision was the most efficacious treatment modality [2••, 25••].

Vesicourethral Anastomotic Stenosis - Incision and Resection

A relatively contemporary series of 50 consecutive patients with BNC treated by a reconstructive urologist with dilation followed by Collings knife lateral incisions quoted a 72% success rate after one procedure and 86% after two procedures. The cohort was a mix of first time and redo procedures with 78% who previously had at least one BNC treatment. Its relevance to VUAS specifically is not clear as the cohort was a mix of post-TURP BNCs and VUASs [26]. The results may be translatable, as a series of VUASs treated with cold knife incisions alone resulted in a 74% success rate, determined by follow up uroflowmetry, in 43 patients after a single procedure. Some caution should be taken in interpretation as there was no cystoscopic confirmation of cure and relatively low flow rates were accepted as normal [24].

Alternatives to transurethral incision are transurethral resection or vaporization. Only small retrospective cohorts are available to evaluate the efficacy of these treatment modalities so results should be interrupted with caution. A small cohort treated with circumferential bipolar resection of VUASs quotes a 91% success rate. Laser vaporization of the obstructing scar tissue, either circumferentially or anteriorly from 3 to 9 o'clock have also been described with efficacies between 76 and 100% with one treatment [27, 28].

Vesicourethral Anastomotic Stenosis - Urethral Dilation and Stents

Small series have suggested that incision could be replaced by high pressure balloon dilation to break the annular fibers of scar tissue. Eight of ten patients treated with dilation alone to 30 French at 30 atm showed no recurrence after a single treatment and the two failures responded to a second identical treatment [29, 30].

Refractory cases of VUAS have previously been managed with urethral stent insertion (Urolume®). In 25 patients who had all undergone endoscopic treatment attempts in the past, a single stent resulted in patency rate of 52%. An additional 24% were salvaged with a second stent placement [31]. These results are relatively inconsequential after the Urolume® stent was removed from the market.

Table 2 Success of endoscopic treatment of VUAS, without the use of adjunctive anti-fibrotic agents, by treatment modality. Pretreatment rate is defined as the patient having undergone a prior endoscopic attempt at VUAS management. (NR - not reported, N/A - not applicable)

Series	Year	Endoscopic Technique	Patients (n)	Pretreatment rate (%)	Success rate - intial treatment (%)	Success rate - multiple treatments (%)
Giannarini & Selli	2007	Cold knife incision	43	0	74	100
Ramirez & Morey	2013	Cold knife incision	50	78	72	86
Kumar & Nargund	2007	Balloon dilation	9	0	89	NR
Ishii & Egawa	2015	High pressure balloon dilation	10	0	80	100
Brodak & Holub	2010	Bipolar transurethral resection	22	NR	91	NR
Lagerveld & de la Rosette	2005	Holmium:YAG laser ablation	10	60	100	N/A
Magera & Elliott	2009	Urethral stent	25	100	52	76
LaBossiere & Rourke	2016	Combined modalities	142	NR	44	91

Adjunctive Maneuvers to Improve Endourologic Outcomes

The limited efficacy of urethral dilation and DVIU led investigators to consider transurethral administration of anti-fibrotic and anti-inflammatory medications. The agents that have been most pervasive in clinical use and subject of the most, though relatively limited, study have been the steroid triamcinolone and Mitomycin C (MMC).

Triamcinolone (80 mg) injection, in conjunction with holmium laser incision, in VUAS that had recurred after initial dilation or DVIU had a reported efficacy of 83% in 24 patients at 2 years of follow up. The purported mechanism of action was enhancement of endogenous collagenase activity by the steroid injection [19].

Mitomycin C has been the subject of more extensive experience and investigation. MMC is a DNA alkylating agent and crosslinker. When administered at a site of potential scar formation, such as after a DVIU, the normal expression of extracellular matrix (ECM) genes is inhibited and fibroblasts undergo apoptosis. The ultimate result is a decreased rate of ECM deposition and slower, less exuberant, scar formation [32, 33].

Unfortunately, there are no randomized controlled trials of MMC for VUAS in the urologic literature so we are dependent on retrospectively reviewed prospective data and multi-institutional retrospective reviews. The Trauma and Urologic Reconstruction Network of Surgeons (TURNS) retrospectively reviewed data from their participating institutions and concluded there may be limited benefit to MMC at the time of DVIU for recalcitrant BNC. Across 8 sites, 55 patients were retrospectively identified over a 5-year period that had undergone treatment with MMC. Forty-four of the patients had a previous dilation or DVIU. They noted a success rate of 58% after one DVIU with MMC at a median follow-up of 9.2 months as defined by the ability to atraumatically pass a 16Fr flexible cystoscope. Nine of 15 patients who underwent repeat DVIU with MMC showed a durable result at a median of 8.6 months. They therefore quoted an overall success rate of 73% after 2 procedures.

There are several points to note regarding this retrospective study. First, these were a combination of BNCs and not VUASs specifically. Second, there was not a standard approach to DVIU. The procedure was variably performed with a cold knife or with electrocautery. Counterintuitively, the study found that electrocautery resection, which causes a local avascularity, was more successful than cold knife incision (63% vs 50%, $p = 0.03$). Finally, the amount of MMC delivered ranged from 0.4 mg to 10.0 mg. Those who advocate for the use of MMC have not suggested 0.4 mg as an adequate dose to expect efficacy.

Importantly, this research collaborative did note a 7% ($n = 4$) serious adverse event rate. Two patients experienced osteitis pubis with early recurrence of their BNC. A third patient developed a rectourethral fistula (RUF) after DVIU and injection. All three patients had a history of XRT. The fourth patient, unexposed to XRT, had extensive necrosis of their bladder neck and prolonged pain [15].

Our experience over a period of 7 years was originally published in 2011 and updated in 2015. Forty patients underwent DVIU with MMC in 4 quadrants (2, 4, 8, and 10 o'clock) with a cold knife. Depending on the length of the stricture, either 1 or 2 cc of 0.4 mg/ml MMC was injected at the base of each incision. At a median follow up of 20.5 months, a 75% patency rate was found after one procedure and an additional 12.5% of patients had a patent repair after second DVIU and MMC injection. There were no serious adverse events [14, 34–38].

Definitive Surgical Management

If attempts at endoscopic management are exhausted and the patient is a suitable surgical candidate, definitive open repair or urinary diversion should be considered. Reanastomosis has traditionally been accomplished by a retropubic or transperineal approach or a combination of the two. It is a technically difficult surgery performed in a scarred field within close proximity of the rectum and should be approached with caution and by experienced hands. More recently minimally invasive robotic assisted laparoscopic interventions have been described.

Transperineal reanastomosis of the bladder neck has been described in several small series with good efficacy. In a series of 15 patients who had undergone at least 4 prior endoscopic interventions, transperineal reanastomosis was successful in 14 of 15 patients and the single failure was managed successfully by repeat DVIU. A similar series of 12 patients, 25% of which had been treated with salvage or adjuvant radiation, that used a combination of transperineal and transabdominal approaches found a similar patency rate of 92%.

It should be noted that in these cohorts and other similar series a vast majority of patients had substantially worse continence after surgery. Nearly all patients will require AUS placement after reanastomosis; AUS placement is done in a staged approach, after urethral patency has been assured. Authors have variably argued for at least 3–6 months of urethral rest after reanastomosis prior to AUS placement [22, 39–42].

Patency rates after transabdominal robotic assisted laparoscopic repairs are lacking for VUAS specifically. In combined series of BNCs and VUASs proof of principle for a robotic approach has been confirmed. Described techniques include Y-V plasty and scar excision with bladder mucosal advancement. The TURNS published their combined experience of 12 patients with a 75% patency rate as determined by passage of a 17Fr cystoscope and flow rate greater than 15 ml/s [1, 21, 43]. The retropubic robotic assisted approach is a key advancement in the ability to successful reconstruct these complex VUASs. The ability to access deep and narrow spaces with superior visualization and comfort allows for precise dissection and reconstruction of stricture area. The perineal area remains unviolated should a future AUS be necessary.

Vesicourethral Anastomotic Stenosis and Urinary Incontinence

Stress urinary incontinence is a well-known side effect of radical prostatectomy. Vesicourethral anastomotic stenoses can either partially mask SUI or contribute to overflow urinary continence. By acting as an obstructive impediment to leak with Valsalva maneuvers, VUASs can mask the severity of post prostatectomy SUI. Alternatively, overflow incontinence can occur if the obstruction is severe and the patient is in resultant urinary retention. It has also been suggested that the circumferential scarring and rigidity of a VUAS can impact the ability of the external urinary sphincter to contract effectively [1].

In the scenario where a VUAS is contributing to continence, treatment of the VUAS can worsen urinary incontinence. This also holds true if the VUAS involves longer segments of the urethra that impact the EUS. Special consideration should be given to the treatment of VUAS in the post XRT setting where the EUS has been in the radiation field. Treatment in this setting can significantly impact urinary incontinence and it is more hazardous to perform future anti-incontinence procedures.

Most authors suggest a staged approach to managing SUI when there is a VUAS or SUI as a result of VUAS treatment. Some authors who offer simultaneous treatment reserved redo DVIUs with long or dense strictures for a staged approach [44]. Stabilization of the anastomotic stricture for a period of 3–6 months is followed by AUS or male sling placement based on the severity of incontinence. Assurance the VUAS is stable prevents the need to operate transurethrally through a deactivated sphincter which risks erosion. A small series of patients with recurrence after AUS placement were successfully managed after sphincter deactivation with a semi-rigid ureteroscope and laser incision [45].

A series of 33 patients were managed by DVIU followed by AUS or male sling when the stenosis had remained patent for at least 3 months. There was only one erosion even though the series included some radiated patients who are more likely to have AUS complications. Patient continence and satisfaction endpoints were not quoted. Similarly, in a series of 21 AUS placements 3 months after DVIU the authors found an 86% success rate as defined by an open anastomosis and urinary continence [23, 46]. Staged management by stabilization of the VUAS with a period to confirm stabilization followed by an anti-incontinence procedure can be effective.

Future Directions

Most contemporary novel management techniques for VUASs focus on anti-fibrotic medication delivery to prevent recurrence after endoscopic management. Studies addressing the specific issue of VUAS with tissue engineering or acellular matrices are lacking. Extrapolating from the urethral stricture literature these technologies are in development and can likely be applied to VUASs.

Phase III clinical trials are underway using a paclitaxel coated balloon for dilation of urethral strictures. Improved outcomes were found with paclitaxel and dilation than dilation alone in the Phase I-II study. A dilation balloon is covered with paclitaxel in a proprietary coating that adheres to the urothelium. The paclitaxel and coating detach at the time of balloon inflation and mucosal contact. The paclitaxel and coating agent adheres to the urothelium allowing for prolonged contact and drug delivery [47]. Transurethrally administered captopril gel has also been shown in a Phase II clinical trial to decrease the rate of stricture after DVIU [48].

Tissue engineering is another novel area of investigation that could ultimately provide exciting results. Acellular matrices have been used to both allow urothelium ingrowth when implanted in the urethra or as a scaffold to create large autologous buccal mucosa grafts with promising results [49, 50]. Tubularized tissue-engineered autologous urethras composed of a muscle and epithelial layer were implanted into 5 human subjects and patency was noted over a media follow-up of 71 months [51, 52].

Conclusions

Vesicourethral anastomotic stenosis after the treatment of prostate cancer is a challenging complication for both patients and urologists. Endoscopic management is not universally effective though success rates do improve with adjunctive measures such as transurethral injection of scar modulating agents. Definitive repair is technically demanding and may result in worsened incontinence necessitating AUS placement. Radiation, before or after prostatectomy, limits the success of endoscopic and formal reconstruction. Targeted intervention of the scar tissue formation and propagation pathway with transurethrally administered medications, represents an exciting possibility to improve success rates with limited patient morbidity. Prospective randomized trials are needed to clarify optimal treatment.

Compliance with Ethical Standards

Conflict of Interest Thomas W. Fuller, Eileen R. Byrne, and Jill C. Buckley declare they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Abbreviations VUAS, Vesicourethral anastomotic stenosis; BNC, Bladder neck contractures; RALP, Robotic assisted laparoscopic prostatectomy; RRP, Radical retropubic prostatectomy; DVIU, Direct visual internal urethrotomy; MMC, Mitomycin C; DNA, Deoxyribonucleic acid; BMG, Buccal mucosa graft; AUS, Artificial urinary sphincter; XRT, External beam radiation therapy; TURNS, Trauma and reconstructive network of surgeons; SEER, Surveillance, epidemiology, and end results; DVC, Dorsal venous complex; RUF, Rectourethral fistula; EUS, External urinary sphincter

References

Papers of particular interest, published recently, have been highlighted as:
•• Of major importance

1. King T, Almallah YZ. Post-radical prostatectomy urinary incontinence: The management of concomitant bladder neck contracture. Adv Urol. 2012;295798.
2.•• LaBossiere JR, Cheung D, Rourke K. Endoscopic treatment of vesicourethral stenosis after radical prostatectomy: outcomes and predictors of success. J Urol. 2016;195(5):1495–500 **A retrospective review of radical prostatectomies over a 10-year period identified 142 patients with VUASs managed endoscopically. The success rate of single transurethral procedure was 44.2%. Ultimately, 91% were managed successfully with multiple procedures.**
3. Browne BM, Vanni AJ. Management of urethral stricture and bladder neck contracture following primary and salvage treatment of prostate cancer. Curr Urol Rep. 2017;18(10):76.
4. Gotto GT, Yunis LH, Vora K, Eastham JA, Scardino PT, Rabbani F. Impact of prior prostate radiation on complications after radical prostatectomy. J Urol. 2010;184(1):136–42.
5. Hu JC, Gu X, Lipsitz SR, Barry MJ, D'Amico AV, Weinberg AC, et al. Comparative effectiveness of minimally invasive vs open radical prostatectomy. JAMA. 2009;302(14):1557–64.
6. Elliott SP, Meng MV, Elkin EP, McAninch JW, Duchane J, Carroll PR. CaPSURE Investigators. Incidence of urethral stricture after primary treatment for prostate cancer: Data from CAPSURE. J Urol. 2007;178(2):529–34.
7. Borboroglu PG, Sands JP, Roberts JL, Amling CL. Risk factors for vesicourethral anastomotic stricture after radical prostatectomy. Urology. 2000;56(1):96–100.
8. Sandhu JS, Gotto GT, Herran LA, Scardino PT, Eastham JA, Rabbani F. Age, obesity, medical comorbidities and surgical technique are predictive of symptomatic anastomotic strictures after contemporary radical prostatectomy. J Urol. 2011;185(6):2148–52.
9. Breyer BN, Davis CB, Cowan JE, Kane CJ, Carrol PR. Incidence of bladder neck contracture after robot-assisted laparoscopic and open radical prostatectomy. BJU Int. 2010;106(11):1734–8.
10. Parihar JS, Ha YS, Kim IY. Bladder neck contracture-incidence and management following contemporary robot assisted radical prostatectomy technique. Prostate Int. 2014;2(1):12–8.
11. Park R, Martin S, Goldberg JD, Lepor H. Anastomotic strictures following radical prostatectomy: insights into incidence, effectiveness of intervention, effect on continence and factors predisposing to occurrence. Urology. 2001;57(4):742–6.
12. Erickson BA, Meeks JJ, Roehl KA, Gonzalez CM, Catalona WJ. Bladder neck contracture after retropubic radical prostatectomy: Incidence and risk factors from a large single-surgeon experience. BJU Int. 2009;104(11):1615–9.
13. Webb DR, Sethi K, Gee K. An analysis of the causes of bladder neck contracture after open and robot-assisted laparoscopic radical prostatectomy. BJU Int. 2009;103(7):957–63.
14. Vanni AJ, Zinman LN, Buckley JC. Radial urethrotomy and intralesional mitomycin C for the management of recurrent bladder neck contractures. J Urol. 2011;186(1):156–60.
15. Redshaw JD, Broghammer JA, Smith TG 3rd, Voelzke BB, Erickson BA, McClung CD, et al. Intralesional injection of mitomycin C at transurethral incision of bladder neck contracture may offer limited benefit: TURNS Study Group. J Urol. 2015;193(2):587–92.

16. Nagpal K, Zinman LN, Lebeis C, Vanni AJ, Buckley JC. Durable results of Mitomycin C injection with internal urethrotomy for refractory bladder neck contractures: Multi-institutional experience. Urol Pract. 2015;2(5):250–5.
17. Mougin J, Souday V, Martin F, Azzouzi AR, Bigot P. Evaluation of hyperbaric oxygen therapy in the treatment of radiation-induced hemorrhagic cystitis. Urology. 2016;94:42–6.
18. Nakada T, Nakada H, Yoshida Y, Nakashima Y, Banya Y, Fujihira T, et al. Hyperbaric oxygen therapy for radiation cystitis in patients with prostate cancer: a long-term follow-up study. Urol Int. 2012;89(2):208–14.
19. Eltahawy E, Gur U, Virasoro R, Schlossberg SM, Jordan GH. Management of recurrent anastomotic stenosis following radical prostatectomy using holmium laser and steroid injections. BJU Int. 2008;102(7):796–8.
20. Raheem OA, Liss MA, Buckley JC. Therapeutic use of Mitomycin C for urological conditions: Systematic review of the literature. Urol Pract. 2016;3(4):283–8.
21. Kirshenbaum EJ, Zhao LC, Myers JB, Elliott SP, Vanni AJ, et al. Patency and incontinence rates after robotic bladder neck reconstruction for vesicourethral anastomotic stenosis and recalcitrant bladder neck contractures: the Trauma and Urologic Reconstructive Network of Su rgeons experience. Urology. 2018;118:227–33.
22. Nikolavsky D, Blakely SA, Hadley DA, Knoll P, Windsperger AP, Terlecki RP, et al. Open reconstruction of recurrent vesicourethral anastomotic stricture after radical prostatectomy. Int Urol Nehprol. 2014;46(11):2147–52.
23. Brede C, Angermeier K, Wood H. Continence outcomes after treatment of recalcitrant postprostatectomy bladder neck contracture and review of the literature. Urology. 2014;83(3):648–52.
24. Giannarini G, Manassero F, Mogorovich A, Valent F, De Maria M, Pistolesi D, et al. Cold-knife incision of anastomotic strictures after radical retropubic prostatectomy with bladder neck preservation: Efficacy and impact on urinary continence status. Eur Urol. 2008;54(3):647–56.
25.•• Song J, Eswara J, Brandes SB. Postprostatectomy anastomosis stenosis: a systematic review. Urology. 2015;86(2):211–8 **A systematic review of postprostatectomy anastomosis stenosis including 22 articles that detailed the success rate of endourologic and open management of VUASs.**
26. Ramirez D, Zhao LC, Bagrodia A, Scott JF, Hudak SJ, Morey AF. Deep lateral transurethral incisions for recurrent bladder neck contracture: Promising 5-year experience using a standardized approach. Urology. 2013;82(6):1430–5.
27. Lagerveld BW, Laguna MP, Debruyne FM, De La Rosette JJ. Holmium:YAG laser for treatment of strictures of vesicourethral anastomosis after radical prostatectomy. J Endourol. 2005;19(4):497–501.
28. Brodak M, Kosina J, Pacovsky J, Navratil P, Holub L. Bipolar transurethral resection of anastomotic strictures after radical prostatectomy. J Endourol. 2010;24(9):1477–81.
29. Ishii G, Naruoka T, Kasai K, Hata K, Omono H, Suzuki M, et al. High pressure balloon dilation for vesicourethral anastomotic strictures after radical prostatectomy. BMC Urol. 2015;15:62.
30. Kumar P, Nargund VH. Management of post-radical prostatectomy anastomotic stricture by endoscopic transurethral balloon dilatation. Scan J Urol Nephrol. 2007;41(4):314–5.
31. Magera JS Jr, Inman BA, Elliott DS. Outcome analysis of urethral wall stent insertion with artificial urinary sphincter placement for severe recurrent bladder neck contracture following radical prostatectomy. J Urol. 2009;181:1236–41.
32. Simman R, Alani H, Williams F. Effect of mitomycin C on keloid fibroblasts: An in vitro study. Ann Plast Surg. 2003;50(1):71–6.
33. Ferguson B, Gray SD, Thibeault S. Time and dose effects of mitomycin C on extracellular matrix fibroblasts and proteins. Laryngoscope. 2005;115(1):110–5.
34. Nagpal K, Zinman LN, Lebeis C, Vanni AJ, Buckley JC. Durable results of mitomycin C injection and internal urethrotomy for refractory bladder neck contractures: Multi-institutional experience. Urol Pract. 2015;2:250–5.
35. Raheem OA, Buckley JC. Adjunctive maneuvers to treat urethral stricture: A review of the world literature. Transl Adrol Urol. 2014;3(2):170–8.
36. Mazdak H, Meshki I, Ghassami F. Effect of mitomycin C on anterior urethral stricture recurrence after internal urethrotomy. Eur Urol. 2007;51(4):1089–92.
37. Sourial MW, Richard PO, Bettez M, Jundi M, Tu LM. Mitomycin-C and urethral dilation: A safe, effective and minimally invasive procedure for recurrent vesicourethral anastomotic stenoses. Urol Oncol. 2017;35(12):672.e15–9.
38. Farrell MR, Sherer BA, Levine LA. Visual internal urethrotomy with intralesional mitomycin C and short-term clean intermittent catheterization for the management of recurrent urethral strictures and bladder neck contractures. Urology. 2015;85(6):1494–9.
39. Simonato A, Gregori A, Lissiani A, Carmignani G. Two-stage transperineal management of posterior urethral strictures or bladder neck contractures associated with urinary incontinence after prostate surgery and endoscopic treatment failures. Eur Urol. 2007;52(5):1499–504.
40. Reiss CP, Pfalzgraf D, Kluth LA, Soave A, Fisch M, Dahlem R. Transperineal reanastomosis for the treatment for highly recurrent anastomotic strictures as a last option before urinary diversion. World J Urol. 2014;32(5):1185–90.
41. Simonato A, Gregori A, Lissiani A, Varca V, Carmignani G. Use of Solovov-Badenoch principle in treating severe and recurrent vesico-urethral anastomosis stricture after radical retropubic prostatectomy: Technique and long-term results. BJU Int. 2012;110(11 Pt B):E456–60.
42. Pfalzgraf D, Beuke M, Isbarn H, Reiss CP, Meyer-Moldenhauer WH, Dahlem R, et al. Open retropubic reanastomosis for highly recurrent and complex bladder neck stenosis. J Urol. 2011;186(5):1944–7.
43. Musch M, Hohenhorst JL, Vogel A, Loewen H, Krege S, Kroepfl D. Robot-assisted laparoscopic Y-V plasty in 12 patients with refractory bladder neck contracture. J Robot Surg. 2018;12(1):139–45.
44. Anger JT, Raj GV, Delvecchio FC, Webster GD. Anastomotic contracture and incontinence after radical prostatectomy: a graded approach to management. J Urol. 2005;173(4):1143–6.
45. Weissbart SJ, Chughtai B, Elterman D, Sandhu JS. Management of anastomotic stricture after artificial urinary sphincter placement in patients who underwent salvage prostatectomy. Urology. 2013;82(2):476–9.
46. Bang SL, Yallappa S, Dalal F, Almallah YZ. Post prostatectomy vesicourethral stenosis or bladder neck contracture with concomitant urinary incontinence: Our experience and recommendations. Curr Urol. 2016;10:32–9.
47. Re-establishing flow via drug coated balloon for the treatment of urethral stricture disease (ROBUST-II). (2017) Retrieved from https://clinicaltrials.gov/ct2/show/NCT03270384 (Identification No. NCT03270384).
48. Shirazi M, Khezri A, Samani SM, Monabbati A, Kojoori J, Hassanpour A. Effect of intraurethral captopril gel on the recurrence of urethral stricture after direct vision internal urethrotomy: Phase II clinical trial. Int J Urol. 2007;14(3):203–8.
49. Osman NI, Hillary C, Bullock AJ, MacNeil S, Chapple CR. Tissue engineered buccal mucosa for urethroplasty. Progress and future directions. Drug Deliv Rev. 2015;82–83:69–76.

50. Pearlman AM, Mujumdar V, McAbee KE, Terlecki RP. Outcomes of adult urethroplasty with commercially available acellular matrix. Ther Adv Urol. 2018;10(11):351–5.
51. Raya-Rivera A, Esquiliano DR, Yoo JJ, Lopez-Bayghen E, Soker S, Atala A. Tissue-engineered autologous urethras for patients who need reconstruction: an observational study. Lancet. 2011;377(9772):1175–82.
52. Versteegden LRM, de Jonge PKJD, IntHout J, Van Kuppevelt TH, Oosterwijk E, et al. Tissue engineering of the urethra. A systematic review and meta-analysi of preclinical and clinical studies. Eur Urol. 2017;72(4):594–606.