

Bladder neck contracture

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Abstract: Bladder neck contracture (BNC) is a well-described complication of the surgical treatment of benign and malignant prostate conditions. Nevertheless, etiologies of BNC development are highly dependent on the primary treatment modality undertaken with BNC also occurring after pelvic radiation. The treatment options for BNC can range from simple, office-based dilation procedures to more invasive, complex abdomino-perineal reconstructive surgery. Although numerous strategies have been described, a patient-specific approach is usually necessary in the management of these complex patients. In this review, we highlight various therapeutic maneuvers described for the management of BNC and further delineate a tailored approach utilized at our institution in these complicated patients.

Keywords: Bladder neck contracture (BNC); prostate cancer; refractory

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Introduction

Bladder neck contracture (BNC) is a well-described complication that may occur following the surgical treatment of benign and malignant prostate conditions. Unfortunately, BNC recurrence after treatment is a common problem even though many series report early success (1-6). Synonymous with vesicourethral stenosis, BNC can range in complexity from simple, short, annular contractures to obliterative stenoses refractory to repeated treatments. Treatment of BNC requires a tailored approach and can range from simple, office-based procedures to complex surgical reconstruction. In this review, we examine various management strategies employed for patients with BNC.

Background

Incidence of BNC

Despite a growing number of patients treated for prostate cancer with either radiation or surgery (7), a relatively small proportion of patients develop BNC warranting further procedural intervention (8-10). Prior to the robotic surgical era, BNC was commonly observed after open retropubic

prostatectomy (11,12). However, robotic surgery has led to a significant decrease in the incidence of BNC, most likely due to improved visualization and exposure at the time of vesicourethral anastomosis. Impressively, recent series from large volume robotic centers report BNC rates approaching zero (5,8,9,11-15). Other factors such as decreased blood loss and a running anastomosis are potential contributing factors for the decreased BNC rate observed with the robotic platform. BNC may also occur as a complication of the surgical treatment of benign prostatic hyperplasia (BPH). Although conventional transurethral resection of prostate (TURP) has resulted in BNC rates as high as 12.3% (16,17), BNC is relatively uncommon (3-5%) with recently developed BPH treatments, such as plasma vaporization of the prostate (3-5%) (18-21).

Etiology

The etiology, frequency, and complexity of a BNC will vary depending on what treatment occurred prior to its occurrence. For example, BNC which develops as a complication of external beam radiotherapy is thought to be caused by microvascular effects and progressive obliterative

endarteritis of the bladder neck ultimately leading to stenosis (22,23). Conversely, prostatectomy patients likely develop BNC due to technical factors at the level of the vesicourethral anastomosis (i.e., urine leak, hematoma, undue tension). Prevention of post-prostatectomy BNC is best prevented through creation of a watertight, tension-free anastomosis with good mucosal apposition (11).

Risk factors for BNC

Recent efforts have attempted to determine factors predictive of BNC (8,9,11,24,25). An analysis performed from the Cancer of the Prostate Strategic Urologic Research Endeavor database demonstrated that BNC development occurs within 6 months after prostatectomy (26) while primary radiation strictures develop many years following initial treatment. The investigators suggested the differing time course of BNC development in radiation patients likely from progressive radiation induced fibrosis and necrosis (27). Patients undergoing salvage therapy for refractory prostate cancer (e.g., salvage prostatectomy or external beam radiotherapy with brachytherapy) have higher rates of BNC development ranging between 20-30% (28-30).

Risk factors for BNC development after prostatectomy include a history of diabetes mellitus, coronary artery disease, obesity, surgeon experience, surgical technique, and certain post-operative complications (hemorrhage, prolonged urine leak, anastomotic disruption). A multivariable analysis performed by Borboroglu *et al.* revealed advanced age, diabetes mellitus, smoking history, coronary artery disease, increased operative time, and increased operative blood loss all as significant risk factors for BNC (11). Of all risk factors, smoking status at the time of radical prostatectomy (RP) was noted to be the strongest independent predictor for the development of BNC. Smoking, shown to impair wound healing through an attenuation of inflammation, reduction of tissue perfusion, and impairment of remodeling, has also been noted as a strong risk factor towards BNC development at our institution (31). Additional risk factors include primary cancer treatment modality (either RP or brachytherapy with external beam radiotherapy) and increased body mass index (BMI) (26).

Minimally invasive management of BNC

Urethral dilation

Non-invasive, office based treatment is the preferred

initial step in BNC management. Flexible cystoscopy and coaxial dilation followed by periodic self-catheterization with bladder neck dilation is most commonly employed to treat anastomotic strictures and further prevent disease recurrence and progression. Such self-dilation regimens are often initiated on an outpatient basis if the BNC is short, soft, and not obliterated.

There are several reports that have investigated the utility of urethral dilation for BNC. In a small cohort of post-prostatectomy patients (n=32), Park *et al.* successfully managed the majority (n=24, 93%) of patients with urethral dilation and a 3-month course of intermittent catheterization (32). Another series of 48 patients reported successful management with a similar regimen following at least one year of follow-up (33). This option is viable only for well-motivated patients, as self-dilation requires a great deal of tolerance and compliance. Ultimately, many patients will abandon self-dilation regimens, likely due to their negative impact on quality of life (34). Complications of intermittent self-dilation include urinary retention, gross hematuria, infection, false passage, and synchronous urethral stricture.

Endoscopic incision

BNC incision can be performed with a variety of techniques, including cold-knife, electrocautery, laser, hot-knife, and loop resection (2,3,25,35-39). Though performed often by the general urologist, short patient follow-up and small patient cohorts limit the generalizability of traditional endoscopic BNC incisional procedures. Importantly, cold-knife incision of the bladder neck may require multiple treatments with success rates decreasing dramatically in patients undergoing repeat surgical intervention. In a prior report of 52 BNC patients undergoing endoscopic treatment, 42% of patients required at least one repeat procedure, while 11.5% required more than two additional procedures (11).

We recently reported a novel endoscopic procedure for BNC that combines dilation and incision (31,40). The BNC is initially dilated with a 4x24 cm Fr UroMax Ultra™ High Pressure urethral balloon dilator. Next, a 24 Fr resectoscope is passed into the bladder, and an incision is then made at the three and nine o'clock position with a Collings knife (cutting current of 30-50 Volts used). The incisions are carried down to the perivesical fat until there is no resistance on the 24 Fr cystoscope sheath. Hemostasis

is then achieved and a 20 Fr Foley catheter is placed and maintained for a period of 4 to 5 days. Two months postoperatively, office cystoscopy and uroflowmetry are performed to assess bladder neck patency.

Results with this novel technique have been promising. With follow-up over one year, the majority of patients (72%) required only one BNC procedure while an additional 14% achieved success after two procedures (31,40). In this series, we defined treatment success as the ability gain entry to the bladder with a 16 Fr flexible cystoscope at the time of follow-up. Success was achievable in complex BNC, as a majority of the study cohort (78%) had undergone a prior transurethral BNC incision. Though conservative measures, such as urethral dilation or endoscopic incision procedures, may be employed in many patients, more invasive options exist for the most severe cases (11,24,38,41).

Urethral stent

Introduced in 1988 by Milroy for urethral stricture management (42), the UroLume “endoprosthesis” (American Medical Systems, Minnesota, USA) has also been used for recalcitrant BNC. Unfortunately, complications such as obstruction caused by tissue in-growth, stent migration/encrustation, hematuria, and the need for repeat surgery are common and thus, the UroLume has fallen out of favor and is now no longer available in the United States (43-50). Outcomes following stent placement were less than promising, even from high volume institutions. Magera *et al.* reported that 48% of patients treated with UroLume stents followed by AUS placement further required additional procedures with 24% experiencing complete treatment failures (51). Similarly, Erickson *et al.* (52) demonstrated an initial success rate of 47% with UroLume stents but a notable majority (n=19, 57%) required repeat intervention due to complications.

Open reconstruction

Open reconstruction of BNC is performed rarely and only in highly selected patients with recalcitrant obstructions at high volume reconstruction centers. Most published series of operative bladder neck reconstruction are limited by short follow-up and small study size. Thus, the reproducibility of published techniques is limited and unpredictable. Various approaches to open BNC reconstruction include abdomino-perineal, perineal, and transpubic (53-55).

Schlossberg *et al.* were among the first to describe

an abdomino-perineal bladder neck reconstruction technique in two post-prostatectomy patients (53). In their technique, the authors described the need for an inferior pubectomy in order to assist with bladder neck exposure and mobilization. While the investigators reported that maintenance of urinary continence was possible, we have found that preservation of the external urinary sphincter is nearly impossible in complex cases requiring this approach.

Pure perineal approaches to refractory BNC treatment have also been reported. Simonato *et al.* described a staged approach in six patients where posterior urethroplasty was initially performed through a perineal incision followed by delayed AUS placement once patency was achieved (56). Mundy *et al.* reported similar findings, thus emphasizing the importance of stress urinary incontinence (SUI) management with staged AUS implantation (57).

Alternatively, BNC reconstruction through a combined abdomino-perineal approach may provide improved exposure, tissue mobilization, scar excision, and bladder outlet reconstruction (54). AUS placement for *de-novo* SUI remains paramount, for which the timing of implantation can be highly variable (54,56,57). At our institution, we counsel patients to expect SUI after open surgical repair and plan for subsequent trans-corporal AUS implantation approximately 3 months postoperatively.

Novel treatment strategies for recalcitrant BNC

Due to the often-disappointing success rates of traditional endoscopic techniques, some investigators have assessed the utility of transurethral incision followed by injection of antiproliferative agents. Steroid injections have been used in an effort to combat fibrosis, scarring, and decrease BNC recurrence (58). Eltahawy *et al.* recently reported a novel technique of triamcinolone injection after Holmium laser BNC incision with a success rate of 83% in 24 patients (58). In a similar experience, Vanni *et al.* reported success rates approaching 90% with the use of mitomycin C, an agent known to inhibit fibroblast proliferation, collagen deposition, and scar formation (59).

Although these findings are both interesting and promising, concerns over the safety profile of novel injection treatments have been raised. Perivesical necrosis from mitomycin C treatment has been documented and animal studies have further demonstrated impaired urothelial wound healing (60-62). Others have reported life threatening anaphylaxis from steroid injections (63).

SUI following successful BNC treatment

Patients undergoing treatment for BNC must be counseled on the possibility of unmasking SUI after the obstruction is relieved. Although SUI after RP requiring surgical management is rare (64-66), patients may experience SUI at higher rates following successful management of BNC (67). An even higher proportion of patients (25-45%) may experience *de-novo* SUI for BNC following salvage prostatectomy (68,69). Nevertheless, data regarding continence outcomes after transurethral incision of the bladder neck are highly variable as some authors suggest low rates of SUI (3,6,11,36,37) while others have demonstrated much higher incontinence rates (32,35,38).

In our experience, few men present with *de-novo* SUI after endoscopic manipulation of BNC as it is much more common for patients to present with concomitant SUI and BNC (31). The timing of intervention for SUI management after BNC treatment remains an important topic. Like previous investigators (67), we advocate for a latency period following BNC treatment of roughly 2 months to assess bladder neck patency prior to AUS implantation. This approach minimizes the risk of restenosis and thus the need for further bladder neck manipulation after AUS cuff placement, thus avoiding risks of cuff erosion. There is no consensus on the time of delay prior to AUS placement, with some authors waiting 4-6 weeks while others delay further treatment up to 12 months (35,59,67).

In our experience, bladder neck stability is ensured through a cystoscopic evaluation performed at 2 to 3 months after BNC treatment. If SUI is present and the bladder neck accommodates a 16 Fr flexible cystoscope in the office setting, the patient is then offered AUS implantation. In the event a symptomatic, recurrent BNC is noted on evaluation after AUS implantation, repeat transurethral incision of the bladder neck may be needed. This can be carefully performed with a holmium laser advanced through a flexible cystoscope or semirigid ureteroscope (70). Alternatively, AUS cuff removal or uncoupling may be necessary to protect the cuff and underlying urethra from damage due to the larger caliber scopes required for BNC incision or resection (31,40).

Conclusions

BNC is an uncommon but challenging condition treated by general, oncologic, and reconstructive urologists. A comprehensive understanding of the various therapeutic

modalities to treat BNC is necessary. Smokers and those with a history of complicated surgery or radiation for prostate cancer appear to be at the highest risk for BNC while other risk factors include diabetes, advanced age, and coronary artery disease. Endoscopic balloon dilation with incision appears to offer promising results in the management of BNC, though open surgery may be warranted in the most complex, refractory cases. Counseling patients regarding the risk of *de-novo* SUI after BNC treatment is critical to ensure expectations are met.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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