The incidence of urethral stricture and bladder neck contracture with transurethral resection vs. holmium laser enucleation of prostate: A matched, dual-center study

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ABSTRACT

Introduction: Urethral strictures (US) and bladder neck contracture (BNC) are common long-term complications of transurethral prostate surgery. We aimed to compare transurethral resection of the prostate (TURP) and holmium laser enucleation of the prostate (HoLEP) regarding incidence of US or BNC and identify possible risk factors.

Methods: A retrospective review of patients who underwent TURP and HoLEP with followup data of at least one year in two separate institutions was performed. The incidence of postoperative US or BNC in both

KEY MESSAGES

- We compared transurethral resection of the prostate (TURP) and holmium laser enucleation of the prostate (HoLEP) regarding their incidence of urethral strictures (US) or bladder neck contracture (BNC) with matching patients for age and prostate volume and identify possible risk factors.
- The US incidence was comparable, although the incidence within TURP arm was higher with bipolar than monopolar TURP.
- The BNC incidence was 1.87% patients in the HoLEP arm, while none of the patients in the TURP arm developed BNC (statistically insignificant).
- Multivariate analysis showed that larger prostate volume and longer operative time were associated with higher risk of US/BNC.
groups was compared. Bivariate and multivariate analysis of risk factors in both cohorts with US or BNC were performed.

**Results:** The study included 208 patients: 101 and 107 patients in the TURP and HoLEP arms, respectively. The two groups were matched for age and prostate size. Eight (7.92%) and five (4.72%) patients in the TURP arm and HoLEP arm, respectively, developed US (p=0.3423), while two (1.87%) patients in the HoLEP arm had BNC (p=0.2634). Of the eight patients with the US in the TURP arm, six (9.8%) patients had bipolar TURP, while two (5%) patients had monopolar TURP. Multivariate analysis showed that larger prostate volume (hazard ratio [HR] 1.22, 95% confidence interval [CI] 1.05, 1.41, p=0.0066) and longer operative time (HR 1.84, 95% CI 1.76, 1.93, p=0.0015) were associated with risk of US/BNC.

**Conclusions:** There is no significant difference between TURP and HoLEP regarding incidence of US or BNC, although there is a tendency towards a higher rate of US associated with bipolar TURP. Increased prostate volume and operative time are possible risk factors.

**INTRODUCTION**

Urethral strictures (US) and bladder neck contracture (BNC) are unfortunate complications of transurethral prostate surgery. Transurethral surgery is considered the most common cause of iatrogenic urethral stricture, accounting for about 41% of all causes. (1) The US incidence is still considered one of the leading long-term complications following transurethral prostate surgery despite the advancement of multiple minimally invasive techniques for managing enlarged prostate and bladder outlet obstruction. US occurs in 4.5-13% of patients post-transurethral prostate surgery. The most common location for US post transurethral surgery is the bulbomembranous urethra, followed by the fossa navicularis and penile urethra. It is also reported that 0.3-9.7% of transurethral prostate surgery are complicated with BNC. (2-4)

The pathogenesis of US in transurethral surgeries is still unclear but supposed mechanisms include breach of mucosal integrity with repetitive ‘in and out’ movement of the resectoscope, lack of adequate lubrication, electric current leak from resectoscope in case of monopolar or Bi-polar diathermy TURP, or pressure ischemia to the fixed bulbomembranous junction. (5,6) Incidence of urethral stricture is also postulated to be related to multiple factors as type of energy used through the resectoscope, size of adenoma, duration of the surgery, the diameter of the resectoscope, temperature of irrigation fluids, and postoperative infection. (7)

In this study, we aim to compare Transurethral resection of prostates (TURP), either monopolar or Bipolar electrocautery, and Holmium laser enucleation of prostate (HoLEP), regarding the Incidence of urethral stricture or bladder neck contracture and identifying the risk factors for the development of urethral stricture in both modalities.
METHODS
The study included a dual-center joint study. A retrospective charts review of a prospectively maintained database of patients who underwent transurethral resection (TURP) or holmium laser enucleation of the prostate (HoLEP) for bladder outlet obstruction within the duration between July 2017 and June 2020 was performed in 2 separate institutions. Transurethral resection of the prostate (TURP) was performed at Alexandria University Hospital while Holmium laser enucleation and morcellation (HoLEP) was performed at Baylor Scott and White Memorial Hospital. The study included patients with at least 1 year complete follow-up post-surgery. Patients in both groups were matched for age and pre-operative prostate volume. Patients with a previous history of transurethral surgery or prospectively diagnosed prostate cancer were excluded. Also, patients with previous history of US or accidently discovered US during TURP or HoLEP were excluded.

Outcome measures
Preoperative, operative, and postoperative characteristics for both groups were collected. The Incidence of postoperative US or BNC in both groups was compared. The data regarding the characteristics of US and management of the US and BNC patients were collected. Multi-variate analysis of the risk factors in the group of patients with US or BNC was performed.

Statistical analysis
For descriptive statistics, continuous variables were presented as Mean (Standard Deviation, SD) or Median (interquartile range, IQR) according to normality while categorical variables were given as absolute numbers and percentages. Two-sample t-tests were used for univariate analysis of most quantitative variables, where equal and unequal variance assumptions were checked, while Wilcoxon Rank Sums tests were used for variables that did not appear to attain normality. Chi-square tests or Fisher’s Exact tests were used for categorical variables according to the expected cell counts. The significance level was set at a p-value < 0.05.

RESULTS
Data of total 1160 patients was reviewed, 160 and 900 patients in TURP and HoLEP groups respectively. This matched study included only 208 patients with follow up of at least 1-year. In the TURP arm, 101 patients fitted our criteria. In HoLEP arm, 107 age and prostate size-matched patients were included. Within the TURP arm, 61 and 40 patients had Bi-polar electrocautery (plasma-kinetic) and Monopolar electrocautery respectively.

The two groups were comparable for the baseline characteristics of age, prostate size, history of previous catheterization, associated bladder stone, and history of DM while HoLEP group had statistically higher PSA and postvoid residual volume compared to TURP group. (Table1).

All the TURP cases were performed using 26 Fr continuous flow sheath, whereas HoLEP was performed with 26 Fr and 28 Fr sheath in 66 and 41 patients, respectively.
TURP group had statistically significant longer operative time and catheterization time (p=0.0067, 0.01, respectively). HoLEP was associated with incidentally discovered prostate cancer on histopathological examination in 14 patients compared to none of the patients in TURP group (p=0.0002). Among the patients with accidental prostate cancer, 12 and 2 patients had Gleason grade group (GG) 1 and GG 2, respectively; all the patients were subsequently managed by active surveillance.

Eight (7.92%) and five (4.72%) patients in the TURP arm and HoLEP arm respectively developed US (p = 0.3423) while 2 (1.87%) patients in the HoLEP arm had BNC (p=0.2634). Out of the 8 patients with US in the TURP arm, 6 (9.8%) patients had Bi-polar TURP, while 2 (5%) patients had monopolar TURP. At the HoLEP group, out of 5 patients with US, 26 Fr and 28 Fr sheath were used in 1 and 4 patients, respectively. The US was bulbar, bulbo-membranous junction, and penile in 9,2,2 patients, respectively. US/BNC were diagnosed with cystoscopy and retrograde urethrogram usually following lack of improvement or worsening lower urinary tract symptoms post-surgery. US / BNC were diagnosed at a range of 1.5 to 24 months post TURP or HoLEP.

With bivariate analysis, the patients with US/BNC had no statistically significant difference regarding their age (p=0.6484), prostate volume (0.1423), history of previous catheterization (p=0.93), serum PSA(p=0.3967), operative time (p=0.9542), catheterization time (p=0.9557), history of DM (p=0.31), or incidental prostate cancer pathology (p=0.15). Multivariate regression analysis model with multiple factors showed that larger prostate volume (Hazard Ratio= 1.222, 95%CI= (1.057, 1.411), p-value=0.0066) and longer operative time (Hazard Ratio= 1.845, 95%CI= (1.762, 1.937), p-value= 0.0015) were associated with statistically significant risk of US/BNC (Table 3).

Among the patients with US, urethral dilatation under local anesthesia was initially attempted in ten patients. Dilatation under local anesthesia sufficient in the management of urethral stricture in 4 and 3 patients in TURP and HoLEP respectively while internal endo-visual urethrotomy was needed for the management of 3 and 2 patients in the TURP arm and HoLEP arm, respectively. One patient in the TURP arm had urethroplasty for management of recurrent urethral stricture. Patients with BNC post-HoLEP were management with endoscopic bladder neck incision with a satisfying outcome. Follow up duration post diagnosis of US/BNC ranged between 5 and 18 months.

DISCUSSION

The rate of US in TURP is estimated in the range of 1.7 to11.7%. It is postulated in multiple reports that the bipolar TURP may be associated with higher rate of US compared to monopolar TURP; with 6.1% to 8.3% versus 1.9% to 4.2%, respectively. (4,8-11) While studies have reported the incidence of US accompanying HoLEP of 1.4% to 4.4%. (12-14) Rate of BNC post-TURP was reported at range of 0.14% to 9.6%, whereas the incidence post-HoLEP is reported between 0.6% and 5.4%. (11, 15)
To our best of knowledge, the current study is the first to directly compare the TURP and HoLEP regarding the US and BNC complications. Our results have shown statistically comparable incidence of US in TURP group and HoLEP group, 7.9% and 4.7%, respectively (p=0.34). Bi-polar TURP was associated with a statistically insignificant higher rate of urethral stricture compared to monopolar type, 9.8% vs. 5%, respectively (p= 0.37). In comparison, BNC occurred in 0% and 1.9% of TURP group and HoLEP group, respectively (p=0.26). Although fossa navicularis stricture is reported in multiple studies as the 2nd most common site of US post-transurethral surgery, none of the patients in both arms had a stricture at the fossa navicularis. (2,4)

Grechenkov et al. in their retrospective study, have illustrated that a larger diameter of the endoscope, increased prostate volume, repeated urethral catheterization, and previous history of chronic prostatitis were associated with the risk of developing of urethra or bladder neck stricture post-TURP. (16) Tao et al, reported in their TURP series that intraoperative urethral mucosa rupture, lower resection speed and postoperative continuous infection were associated with a higher risk of US while severer storage phase symptom and smaller prostate size were associated with a higher risk of BNC after TURP. (7) Thai et al. found the rate of US and BNC post-HoLEP was comparable with utilizing either a 26-French or 28-French resectoscope sheath. (13) In our results, multivariate analysis showed that longer operative time and larger prostate volume were associated with statistically significant risk of US. According to Ibrahim et al. in their large HoLEP series, BNC developed only in patients with a small adenoma (less than 55 gm), with 60% of BNC patients had history of previous TURP. (14) Lee et al. have also showed that 96% of patients of BNC post-TURP had prostate less than 50 gm. (15) In our results, bladder neck contracture developed in 2 (1.9%) patients in the HoLEP arm with the prostate volume of 45 and 50 gm.

Of note, our results, in contrary to previous studies, showed that HoLEP was associated with shorter operative time compared to TURP. (17) This may be attributed to longer time spent for hemostasis in TURP for large prostates that may compensate for time needed for morcellation during HoLEP.

The management of US post-TURP or HoLEP varies with the site and the length of the stricture segment. Studies reported variable success rates for endoscopic management of US post transurethral surgery. Urethral dilatation under local anesthesia with a balloon, filiform, and followers, urethral sounds or self-dilatation with catheters can be adequate in 50 % to 71%, especially patients with previously untreated strictures and soft annular strictures, while visual internal urethrotomy is required in 20% to 30% of patients, especially with complications or retention (4,14,18) Endoscopic incision of the bladder neck is usually required in patients with BNC with evident success rate. (14, 15)

Limitations
The study's retrospective nature and the relatively small number of patients considering the low incidence of urethral stricture complication. A prospective randomized study with a larger
number of patients is required. However, it will be difficult due to the small incidence of complications.

**CONCLUSIONS**

There is no significant difference between TURP and HoLEP regarding the incidence of US or BNC although there is tendency towards higher rate of US associated with Bi-polar TURP and higher incidence of BNC associated with HoLEP. Larger prostate volume and longer operative time are associated with higher risk of urethral stricture. Endoscopic treatment with urethral dilatation, visual urethrotomy or bladder neck incision is effective management in most of patients.
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Figures and Tables

Table 1. Baseline characteristics of both groups

| Variable                           | TURP (n=101) | HoLEP (n=107) | p  |
|------------------------------------|--------------|---------------|----|
| Age, years, median (IQR)           | 66 (62–80)   | 66 (61–69)    | 0.9668 |
| Prostate size, g, median (IQR)     | 62 (49–83)   | 68 (53–80)    | 0.7112 |
| PSA, ng/ml, median (IQR)           | 2.3 (1.3–4.1)| 4.7 (2.4–7.4) | <0.0001 |
| Hx of urine retention, n (%)       | 33 (32.6%)   | 43 (42%)      | 0.15 |
| DM, n (%)                          | 28 (27.7%)   | 29 (27.1%)    | 0.92 |
| PVR, ml, mean (SD)                 | 43.63 (70)   | 127 (146)     | <0.0001 |
| Bladder stone, n (%)               | 9 (8.9%)     | 7 (6.6%)      | 0.21 |

DM: diabetes mellitus; HoLEP: holmium laser enucleation of prostate; Hx: history; IQR: interquartile range; PSA: prostate-specific antigen; PVR: postvoid residual; SD: standard deviation; TURP: transurethral resection of prostate.

Table 2. Perioperative and outcome data

|                              | TURP (n=101) | HoLEP (n=107) | p  |
|------------------------------|--------------|---------------|----|
| Operative time, min, median (IQR) | 88 (71–92)  | 71.1 (58–84) | 0.0067 |
| Catheterization time, days, mean (SD) | 2.12 (0.64) | 1.81 (2.28) | 0.01 |
| Incidental PCa pathology, no (%)   | 0            | 14 (13.8)    | 0.0002 |
| Urethral stricture, no (%)        | 8 (7.92)     | 5 (4.72)     | 0.3423 |
| BN contracture, no (%)           | 0            | 2 (1.87)     | 0.2634 |
| Stricture onset, months, median (IQR) | 8 (6–8)     | 7 (3–14)     | 1.0 |

BN: bladder neck; HoLEP: holmium laser enucleation of prostate; IQR: interquartile range; PCa: prostate cancer; SD: standard deviation; TURP: transurethral resection of prostate.
Table 3. Bivariate analysis of urethral stricture patients vs. noncomplicated patients

| Variable                        | US/BNC (n=15) | No US/BNC (n=193) | p    |
|--------------------------------|---------------|-------------------|------|
| Age, years, median (IQR)       | 65 (61–68)    | 66 (61–70)        | 0.6484 |
| Prostate size, g, median (IQR) | 80 (60–90)    | 63 (50–79)        | 0.1423 |
| PSA, ng/ml, median (IQR)       | 4.6 (3.05–5.4)| 3.4 (1.6–6.1)    | 0.3967 |
| Preoperative urine retention, n (%) | 4 (30%) | 58 (29%) | 0.93 |
| DM, n (%)                      | 5 (38%)       | 50 (26%)          | 0.311 |
| PVR, ml, median (IQR)          | 80 (35–130)   | 37.5 (0–140)      | 0.1854 |
| Operative time, min, median (IQR) | 70 (64.2–75) | 66 (55–80)        | 0.9542 |
| Catheter time, days, median (IQR) | 2 (1–2)    | 2 (1–2)           | 0.9557 |
| PCa pathology, n (%)           | 2 (15%)       | 11 (5.6%)         | 0.15  |

BNC: bladder neck contracture; DM: diabetes mellitus; IQR: interquartile range; PCa: prostate cancer; PSA: prostate-specific antigen; PVR: postvoid residual; US: urethral stricture.