# The Long-term Effects of Transurethral Bladder Neck Incision in the Treatment of Female Bladder Neck Obstruction

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**Purpose:** To investigate the long-term effects of transurethral bladder neck incision (TUBNI) for female primary bladder neck obstruction (PBNO).

Materials and Methods: We retrospectively reviewed seventy women diagnosed with bladder neck obstruction by video-urodynamic study (VUDS). TUBNI was performed for each patient, with incisions made at 2 different sites on the bladder neck. Postoperatively, patients were assessed by international prostate symptom score (IPSS), quality of life (QOL) and uroflowmetry.

**Results:** Follow-up data were available for 4-108 months (median 42 months) postoperatively. During follow-up, the IPSS, QOL, time to maximum uroflow rate, postvoid residual urine volume decreased significantly after TUB-NI compared with preoperative [13.0 (10.0, 15.0) versus 3.0 (3.0, 8.0),  $P \le .001$ ], [5.0 (5.0, 5.0) versus 2.0 (1.0, 3.0),  $P \le .001$ ], [9.0 (5.0, 37.0) versus 6.1 (4.2, 8.7),  $P \le .001$ ], [77.5 (23.5, 165.8) versus 0.0 (0.0, 30.0),  $P \le .001$ ]. The maximum uroflow rate, average uroflow rate and the voided volume increased significantly compared with preoperative [7.0 (4.0, 10.3) versus 19.8 (12.8, 25.2),  $P \le .001$ ], [3.0 (2.0, 5.0) versus 8.0 (4.9, 10.7),  $P \le .001$ ] and [156.5 (85.0, 211.3) versus 261.3 (166.2, 345.6),  $P \le .001$ ]. Several complications were identified after surgery, including bladder neck reobstruction, urethral stricture, and stress urinary incontinence, the corresponding number was 5 (7.1%), 7(10%) and 7(10%). Successful operation was achieved in 60/70 (85.7%) patients.

**Conclusion:** PBNO is a very rare yet easily treatable condition. VUDS is the primary diagnostic tool for the diagnosis of bladder neck obstruction in women, while TUBNI can effectively relieve obstruction symptoms and improve the quality of life for patients.

**Keywords:** female bladder neck obstruction; video-urodynamic study; transurethral bladder neck incision; urinary incontinence; urethral stricture

## INTRODUCTION

Female bladder neck obstruction is an uncommon condition compared with men and is observed in 1%-16% of women deemed to have bladder outlet obstruction. The precise cause of PBNO has not been elucidated and the etiology has been attributed to detrusor bladder neck dyssynergia, bladder neck hypertrophy secondary to a distal urethral obstruction, fibrosis of the bladder neck, striated muscle extends from the external sphincter to the bladder neck, and increased sympathetic activity at the bladder neck. (2,3)

There are numerous causes of bladder outlet obstruction in women, which can generally be divided into anatomical causes and functional causes. Anatomical causes are more common and can be extrinsic (pelvic organ prolapse or post-anti-incontinence procedure), urethral (stricture, meatal stenosis, urethral caruncle, fibrosis or diverticulum) or luminal (stone, bladder or urethral tumor, ureterocele or foreign body)<sup>(4)</sup> Functional obstruction can be diagnosed only during the act of voiding because no obvious anatomic abnormality will be associated with the patient's symptoms. Functional causes may be a consequence of improper external striated sphincter relaxation or contraction during

voiding caused by senile bladder changes, neurological diseases, diabetes mellitus, other peripheral neuropathy, or non-neurogenic causes. The two most common functional causes are dysfunctional voiding (DV) and PBNO.<sup>(5,6)</sup> Although they have similar presentations, their etiology and therapy are completely different. PBNO may present with a variety of symptoms, including voiding or obstructive symptoms (decreased force of stream, hesitancy, intermittent stream, incomplete emptying), storage or irritative symptoms (frequency, urgency, urinary incontinence, nocturia) or a combination of both.<sup>(7)</sup>

PBNO in women is a video-urodynamic diagnosis whose hallmarks include high detrusor pressure (maximal detrusor pressure at the maximum flow rate, Pdet. Qmax > 20cm H<sub>2</sub>O), a low flow rate (maximum flow rate, Qmax <12 ml/s), radiographic evidence of nonfunneling at the bladder neck with the relaxation of the striated sphincter, and no evidence of distal obstruction. (8.9) Treatment options for PBNO include watchful waiting, pharmacotherapy, and surgical intervention. (10) For patients having poor responses to medication, those experiencing severe medicinal side effects, and those who are unwilling or incompetent to perform clean intermittent self-catheterization, TUBNI is a treatment option

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**Table 1.** Clinical data of patients presenting with symptoms.

| Characteristics                    | Number of patients | Percentage |  |  |
|------------------------------------|--------------------|------------|--|--|
| Age, years, mean ± SD              | 54.9±13.5          |            |  |  |
| BMI, kg/m2, mean $\pm$ SD          | 24.3±3.6           |            |  |  |
| Difficult micturition symptoms     | 68                 | 97.1       |  |  |
| Recurrent urinary tract infections | 11                 | 15.7       |  |  |
| Urinary retention                  | 6                  | 8.6        |  |  |
| Perineal or pelvic pain            | 9                  | 12.9       |  |  |
| Combined with SUI                  | 2                  | 2.9        |  |  |
| Combined with urethral stricture   | 5                  | 7.1        |  |  |
| High serum creatinine              | 3                  | 4.3        |  |  |

Abbreviations: SD, Standard deviation; BMI, Body Mass Index; SUI, Stress urinary incontinence.

with excellent therapeutic results. The main concerns of bladder neck incision in females are the development of postoperative stress urinary incontinence (SUI) and urethral stricture. We present a retrospective analysis of treatment in female bladder neck obstruction, with special emphasis on surgical therapy and complications in the post-operative period.

## **MATERIALS AND METHODS**

#### Study population

This study retrospectively collected the data from 70 female patients underwent TUBNI in urology of Beijing Chao-Yang Hospital between April 2012 to December 2020 which collected by the electronic medical record system. All the patients underwent physical examination, a comprehensive medical history, blood routine detection, serum, and urine biochemistry, while all patients filled IPSS and QOL questionnaires. Uroflowmetry was performed in all patients to initially assess the Omax. If Omax <12 ml/s, we tentatively considered the presence of bladder outlet obstruction (BOO). VUDS was performed on all patients to verify the cause of difficult voiding. The most common symptoms on admission included frequency, urgency, difficult micturition, and urinary retention. All patients were treated with α-blockers for at least 1 month. Tamsulosin, prazosin, or terazosin was prescribed at different times, patients who improved after pharmacotherapy were excluded from the study.

# Inclusion and exclusion criteria

Patients were included in the study if they met the inclusion criteria: (I) age > 18 years; (II) VUDS showed Pdet.Qmax > 20cm H<sub>2</sub>O, or Qmax < 12 ml/s; (III) treatment by TUBNI; (IV) Complete medical history

information. Patients with other urinary diseases, such as dysuria caused by neurogenic bladder, urethral neoplasms, urethral diverticulum, and pelvic organ prolapse, or who were unable to complete follow-up were excluded from the study.

#### **Procedures**

Uroflowmetry was performed in all patients for preliminary assessment of maximum urinary flow rate. The postvoid residual (PVR) was measured with ultrasonography (Netherlands, MMS Company, Bladder Scan BVI 6100).

VUDS was performed for all the patients using a Laborie Urodynamic System (Canada, Laborie) and the X-ray (Siemens Access UROSKOP). VUDS was accomplished according to the instructions of the International Continence Society. (11) VUDS was performed with a 6F dual-lumen catheter with an infusion of 15% meglumine diatrizoate at a rate of 20-40 mL/min. The abdominal pressure was recorded with a COOK 8F abdominal pressure tube mounted to a balloon inflated with 5 mL of normal saline. Fluoroscopy of the urinary bladder and the urethra was performed with a C-arm fluoroscope (Siemens Medical Solutions) placed projecting at 45° from the buttock so that the bladder neck and the urethra could be demonstrated properly. After catheterization, the postvoid residual urine was evacuated and measured. VUDS was performed with the patient sitting on a chair, whereas the bladder neck and external sphincter urodynamics were monitored simultaneously using C-arm fluoroscopy. During the filling phase, the patients were asked to cough or other abdominal pressure rises several times to ensure that the abdominal and intravesical pressure signals respond equally. Prevention of liquid leaks and air bubbles in the pressure tubing system is needed throughout testing and should be corrected when identified. When the cystometric capacity was reached, the patients were asked to urinate into the uroflowmeter with the urethral catheter and rectal tube in place. Cine-fluoroscopy was performed during the filling and voiding phases. During the voiding phase, the opening of the bladder neck and the urethra were carefully inspected. Bladder neck obstruction in women was defined as the lack of a 'funnel shape' of the bladder neck during voiding, at the same time with the Pdet.Qmax  $\geq$  20cm H<sub>2</sub>O, or Qmax  $\leq$  12 ml/s.<sup>(9,12-14)</sup>

TUBNI was performed for all the patients. The operation was performed in the lithotomy position and it is performed through a 24-F resectoscope using the bipolar electrode. Endoscopic incisions typically are made

Table 2. Comparison of IPSS, QOL and parameters of uroflowmetry before and after bladder neck incision.

| Parameters <sup>a</sup> | Preoperative       | 95% CI      | Postoperative       | 95% CI      | Z-value             | P-value |
|-------------------------|--------------------|-------------|---------------------|-------------|---------------------|---------|
| IPSS                    | 13.0 (10.0,15.0)   | 12.3-13.8   | 3.0 (3.0,8.0)       | 4.4-6.2     | -6.797 <sup>b</sup> | <.001   |
| QOL                     | 5.0 (5.0,5.0)      | 4.8-5.1     | 2.0 (1.0,3.0)       | 2.2-2.9     | -6.796 <sup>b</sup> | <.001   |
| Qmax (ml/s)             | 7.0 (4.0,10.3)     | 6.6-8.7     | 19.8 (12.8,25.2)    | 18.1-21.9   | -7.254°             | <.001   |
| Qave (ml/s)             | 3.0 (2.0,5.0)      | 2.9-3.9     | 8.0 (4.9,10.7)      | 7.1-8.8     | -6.697°             | <.001   |
| TQmax (s)               | 9.0 (5.0,37.0)     | 22.5-49.1   | 6.1 (4.2,8.7)       | 5.6-10.8    | -4.858b             | <.001   |
| PVR (mL)                | 77.5 (23.5,165.8)  | 79.9-126.2  | 0.0 (0.0,30.0)      | 14.0-34.1   | -5.560 <sup>b</sup> | <.001   |
| Voiding volume (mL)     | 156.5 (85.0,211.3) | 128.4-170.8 | 261.3 (166.2,345.6) | 247.1-312.3 | 4 -5.978°           | <.001   |

Abbreviations: CI, Confidence interval; IPSS, International prostate symptom score; QOL, Quality of life; Qmax, Maximum uroflow rate; Qave, Average uroflow rate; TQmax, Time to maximum uroflow rate; PVR, Postvoid residual urine volume.

<sup>&</sup>lt;sup>a</sup>Data were presented as M(P25, P75) and compared by Wilcoxon Signed Ranks Test.

<sup>&</sup>lt;sup>b</sup>Based on positive ranks.

Based on negative ranks.

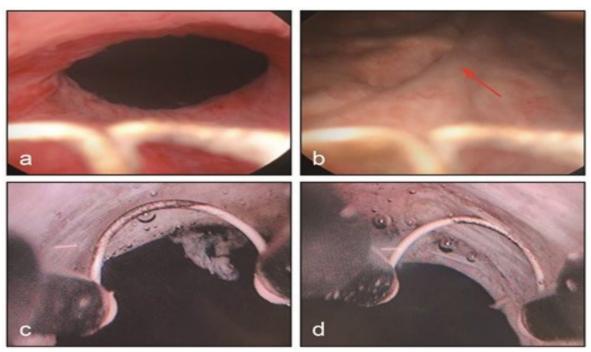


Figure 1. A: Transurethral view during endoscopic incision of the bladder neck in a patient. B: The trabecular structure of the bladder can be seen under endoscope (arrow). C: Transurethral bladder neck incision at 11 o'clock position. D: Transurethral bladder neck incision at 2 o'clock position.

at the bladder neck and proximal urethral at two different positions. In 42 patients, the incision was performed at 3- and 9 o'clock position, and other 28 patients were performed at 1-2 and 10-11 o'clock position. Before making the incision, we utilized a cystoscope to repeatedly check the location of the urethral sphincter, which was situated 1.5-2cm outward from the bladder neck and looked endoscopically as a circular contractable ring. We began by incising open the bladder neck and extending the incision far beyond feasible till no fib-

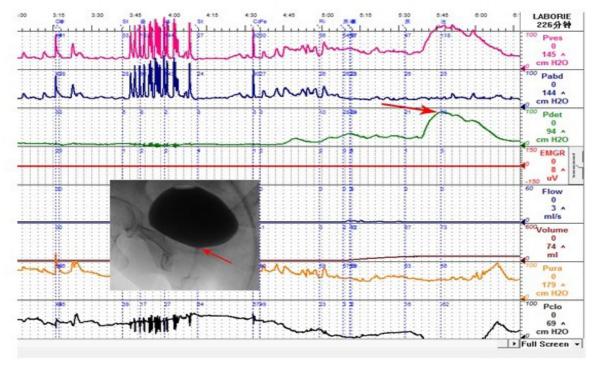


Figure 2. Preoperative VUDS in a patient who presented with difficult micturition symptoms. A radiograph was obtained at the maximum detrusor pressure and showed that the bladder neck did not open as a 'funnel shape' during voiding (arrow), the patient was unable to void and had a detrusor pressure > 90cmH<sub>2</sub>O.

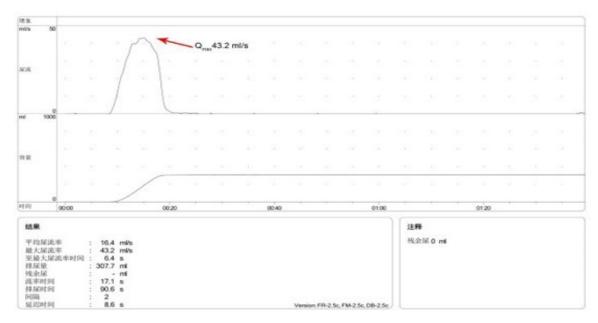


Figure 3. Postoperative uroflowmetry in a patient able to void with a maximum uroflow rate of 43.2 ml/s and postvoid residual urine volume of 0 ml.

er circle could be visible at the bladder neck and the fat could be visualized. Careful should be taken not to damage the external urethral sphincter (Figure 1). A 22F Foley catheter was used for 5-7 days after the operation. Furthermore, patients had bladder neck obstruction combined with SUI, a tension-free vaginal tape (TVT) was performed 3 months after TUBNI if necessary. Urethral dilation before TUBNI was performed for those patients combined with urethral stricture patients.

## **Evaluations**

We contacted all patients by telephone and asked them to revisit our clinic for follow-up examinations. The follow-up IPSS, QOL, uroflowmetry, and all postsurgical complications, such as bladder neck recontracture, urethral stricture, and SUI were all recorded. Pre and post-operative data of IPSS score, QOL score, Qmax, average uroflow rate (Qave), time to maximum uroflow rate (TQmax), postvoid residual urine volume (PVR), and the voided volume in each patient were all compared.

#### Statistical Analysis

Measurement data were tested for shapiro-Wilk normality. Continuous variables with normal distribution were presented as means  $\pm$  standard deviation (SD) and compared by Paired t-test. While continuous variables with non-normal distribution were reported as median with interquartile range (P25, P75) and compared by Wilcoxon signed-rank test. A P value of less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS statistical software version 26.0 (IBM, Chicago, IL, USA).

## RESULTS

A total of 70 female patients underwent complete investigations and follow up. The median follow-up duration was 42 months (range, 4-108). The mean age was 54.9±13.5(95% CI: 51.6-58.1) years and the mean body mass index (BMI) was 24.3±3.6 (95% CI: 23.4-25.2) kg/m<sup>2</sup>. The duration of lower urinary tract symptoms in all patients ranged from 4 month to 30 years (median 4.9 years). **Table 1** lists patient baseline characteristics. Common presenting symptoms include difficult micturition symptoms (n = 68, 97.1%), recurrent urinary tract infections (n = 11, 15.7%), urinary retention (n = 6, 8.6%), perineal or pelvic pain (n = 9, 12.9%), combined with SUI (n = 2, 2.9%), combined with urethral stricture (n = 5, 7.1%), and high serum creatinine (n = 3, 4.3%). A comparison of the preoperative and postoperative data was listed in **Table 2**. The IPSS, QOL, TQmax, and PVR decreased significantly after TUBNI compared with preoperative [13.0 (10.0, 15.0), 95% CI: 12.3-13.8] versus [3.0 (3.0, 8.0), 95% CI: 4.4-6.2], [5.0 (5.0, 5.0), 95% CI: 4.8-5.1] versus [2.0 (1.0, 3.0), 95% CI: 2.2-2.9], [9.0 (5.0, 37.0), 95% CI: 22.5-49.1] versus [6.1 (4.2, 8.7), 95% CI: 5.6-10.8], [77.5 (23.5, 165.8), 95% CI: 79.9-126.2 ] versus [0.0 (0.0, 30.0), 95% CI: 14.0-34.1] (all  $P \le .001$ ). The Qmax, the Qave and the voided volume increased significantly [7.0 (4.0, 10.3), 95% CI: 6.6-8.7] versus [19.8 (12.8, 25.2), 95% CI: 18.1-21.9], [3.0 (2.0, 5.0), 95% CI: 2.9-3.9] versus [8.0 (4.9, 10.7), 95% CI: 7.1-8.8] and [156.5 (85.0, 211.3), 95%CI: 128.4-170.8] versus [261.3 (166.2, 345.6), 95% CI: 247.1-312.34] (all  $P \le .001$ ).

VUDS revealed the simultaneous presence of high detrusor pressure and low flow rate, and synchronous fluoroscopy indicated that the bladder neck did not open adequately (remained closed or narrow on fluoroscopic images) during voiding. The maximal detrusor pressure at the maximum uroflow rate was 38.5 (28.0-64.5) cmH2O. The Qmax was 7.0 (4.0, 10.3) ml/s. All patients presented with non-funnel bladder neck during voiding. After the TUBNI procedure, follow-up uroflowmetry showed that the patient's condition was improving meaningfully, and we considered Qmax greater than 12ml/s to indicate that the operation was success-

ful. (Figures 2 and 3).

Several complications were identified after surgery, including bladder neck recontracture, urethral stricture, and SUI. 5 (7.1%) women underwent multiple TUB-NIs because of recurrent bladder neck obstruction, of these, a second TUBNI was performed in 4 patients, and a third TUBNI was performed in 1 patient. The second and third incisions were made in the same positions as the first, all these patients experienced alleviation of their difficult voiding symptoms after repeated TUB-NI. 7 (10%) patients experienced urethral stricture after TUBNI and 6 were relieved after receiving intermittent urethral dilation. 7 (10%) patients suffered from SUI, of which 4 slight symptom patients were relieved after Kegel exercises, and 3 severe patients refused to have the second surgery due to poor body condition and chose to wear the diaper.

Finally, symptoms were not ameliorated in 10 of 70 (14.3%) patients, including 3 with SUI and 1 with urethral stricture, 6 patients experienced no significant postoperative relief in spite of no complications occurred.

## **DISCUSSION**

The understanding of the presentation, diagnosis, and treatment of PBNO has developed over the last 20 years. PBNO is a functional condition that is caused by inadequate bladder neck that open during voiding, the features are low flow and high pressure. Nevertheless , many women void normally with low detrusor pressures (less than 10 cmH<sub>2</sub>O) and can empty the bladder with a good urinary flow rate, which may in part be since many women void by pelvic relaxation or abdominal straining (by habit) without needing to generate significant detrusor pressures. (13) Therefore, the diagnosis criteria for women and men were not completely uniform. In women, there is no consensus regarding a cutoff for detrusor pressure and flow rate diagnostic of obstruction, although some have defined it based on urodynamic parameters. (1,13) Since 1998, a series of criteria have been proposed. Chassange et al. (14) proposed the first cut points for obstruction, Qmax 15 ml/s, and Pdet.Qmax > 20 cm H<sub>2</sub>O. Groutz et al. (8) defined the criteria as Qmax < 12 ml/s and Pdet. Qmax > 20 cm H<sub>2</sub>O. Gammie et al. (15) used Qmax < 12 ml/s and Pdet.  $Q^2$ max  $\geq$  40 cm H2O to define the presence of obstruction. However, VUDS is the most accurate method for the diagnosis of female bladder neck obstruction. In our study, the diagnostic criteria were Pdet.Omax > 20cm H<sub>2</sub>O, Qmax <12 ml/s, or radiographic evidence of nonfunneling at the bladder neck during voiding.

Treatment options for PBNO in females included watchful waiting, pharmacotherapy, and surgical intervention. Clean intermittent self-catheterization or α-blockers is the first-line treatment, if therapy becomes necessary. The next therapeutics possibility is the transurethral incision of the bladder neck. (16) Transurethral incision seem to be the preferred treatment with the expectation of eminent results. However, no agreement has been reached on where to cut the bladder neck in women. Turner-Warwick et al.(17) first described the concept of bladder neck incision in 1973, they made a single midline incision anteriorly to avoiding the risk of subsequent fistulation into the vaginal vault, which can follow posterior or posterolateral incision. Kumar et al.<sup>(18)</sup> chose a single incision was made at the 12 o'clock position from 2 mm proximal to the bladder neck to the mid urethra. They reported the 6 patients who underwent bladder neck incision showed dramatic improvement in symptoms, peak flow, and post-void residual. However, 3 patients (50%) underwent a repeat TUBNI after 12 months because their symptoms recurred. These results implied that TUBNI is an effective treatment for female with bladder neck obstruction, but, a single incision at the 12-o'clock position could not thoroughly relieve the obstruction. Blaivas et al. (1) chose the 5- and 7-o'clock positions as the incision site. 6 patients (85.7%) considered themselves cured of lower urinary tract symptoms and 1 was improved, and these authors did not report complications of vaginal wall injuries. Peng et al. (19) also chose the 5- and 7-o'clock positions as the incision site. They reported the overall satisfactory rate was good (91%), but several patients suffered urethral- Vaginal fistula.

As we were cautious that a single incision would not adequately relieve the obstruction, we performed 2 different incisions for all of the patients in our study, and none of them developed a vesicovaginal fistula postsurgical. 60/70 (85.7%) patients were considered to have successfully recovered after the TUBNI. Moreover, in our study, 2 (2.9%) patients had PBNO combined with SUI before the surgery, their obstruction symptoms were relieved after TUBNI. They were assessed symptoms and uroflowmetry at 3 months postoperatively, IPSS decreased from 16 to 1 and 6 to 3 respectively, Qmax improved 6 ml/s to 23.5 ml/s and 10 ml/s to 30.7 ml/s respectively. Then TVT was performed for two women and their leakage symptoms were also relieved successfully after second operation as planned. Therefore, we recommend that TUBNI and TVT should be performed sequentially for those patients who have both PBNO and SUI, and good results could be expected. 5 (7.1%) patients combined with urethral stricture before the TUBNI. These patients were performed several urethral dilations before and after TUBNI, these individuals underwent several urethral dilation procedures and their symptoms were successfully addressed. In our experience, TUBNI combination with urethral dilation is an excellent treatment for females with PBNO combined with urethral stricture. Furthermore, of 70 patients, 3 had high serum creatinine. Kumar et al. (20) studied 13 patients who presented in renal failure with obstructive voiding symptoms or retention. The symptoms were relieved with the help of  $\alpha$ -blockers, bladder neck incision, and clean intermittent self-catheterization. They suggested that bladder neck obstruction is a rare cause of renal failure which can be corrected if treated appropriately. Notably, 3 patients had high serum creatinine levels before surgery, and 6 had urinary retention, and their serum creatinine levels returned to normal after TUBNI. We considered that elevated creatinine may be associated with more severe BOO and a longer duration of BOO. The urinary retention makes the patient vulnerable to infection, which further deteriorates renal function. Proper TUBNI can relieve the PBNO and protect renal function.

Several complications postsurgical were identified in this study, including bladder neck reobstruction, ure-thral stricture, and SUI. Five patients suffered reobstruction of the bladder neck post TUBNI, while their symptoms were relieved after multiple TUBNIs. Seven (10%) patients experienced urethral stricture after TUBNI and 6 were alleviated after consecutive urethral

dilations. SUI was indeed the main complication. Overzealous therapy has been attributed to incontinence in numerous studies. The external urethral sphincter must be identified when the incision is performed. The most prevalent complication of striated sphincter damage is urinary incontinence. The incision should be restricted to the proximal third of the urethra, and it should be carefully controlled. This could be beneficial for preventing urinary incontinence. (18) SUI are highly prevalent among women, especially in older women, and SUI is associated most often with pelvic floor muscle laxity. Multiple risk factors have been proposed and studied for the development of SUI in women, such as age, obesity body index, vaginal delivery, and hormone replacement therapy. (21-23) Cavkaytar et al. (24) reported that Kegel exercises have been found effective in women with urinary stress and mixed incontinence, and the improvement was more prominent in women with SUI. In our group, 7 (10%) patients suffered from mild SUI after operation. The age was 68.8 (range 55-82) years. The mean BMI was 27.6 (range 24-35.7) kg/m<sup>2</sup>. These results suggest that age and obesity may be risk factors for SUI after TUBNI. Although the external urethral sphincter was not damaged during TUBNI, these post-operative SUI patients did not show obvious leakage symptoms before TUBNI. We deduced that the obvious bladder neck resistance covered SUI symptoms, and that once the resistance was removed by TUBNI, the urinary incontinence that should have occurred became obvious. After exercising Kegel exercises, four patients with minor symptoms were all relieved. The remaining three patients, who refused the second procedure due to their terrible physical situation, were required to wear diapers. These were the problems we need to solve in the feture.

#### **CONCLUSIONS**

Primary bladder neck obstruction is one of the commonest causes of lower urinary tract symptoms in women. Although bladder neck obstruction has non-specific manifestations, the main symptoms including voiding, obstructive, storage and irritative symptoms. The diagnosis of bladder neck obstruction in women can be successfully made by uroflowmetry, cystoscopy, and Video-urodynamic study combined with clinical presentation. Transurethral bladder neck incision is an effective therapy for bladder neck obstruction. Careful, sufficiently deep incisions at 2 different positions can ensure its success, and attention should be paid to complications such as bladder neck reobstruction, urethral stricture, and stress urinary incontinence. To the best of our knowledge, this is a relatively large sample of patients with bladder neck obstruction who underwent transurethral bladder neck incision with few complications. Ultimately, we recommend that long-term postoperative follow-up and positive treatment of related complications should be performed.

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# **CONFLICT ON INTEREST**

The authors reportt no conflict of interest.

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