Transurethral Incision of the Bladder Neck with Additional Procedure Resumes Spontaneous Voiding in Female Voiding Dysfunction – A Long-term Follow-up

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Abstract

Introductions: To evaluate the long-term effectiveness of transurethral incision of the bladder neck (TUI-BN) with or without additional procedure for female voiding dysfunction.

Methods: Women with voiding difficulty and underwent TUI-BN in recent 12 years were included. All patients underwent videourodynamics study (VUDS) at baseline and after TUI-BN. Successful outcome was defined as having a voiding efficiency (VE) by ≥50% after treatment. Patients with insufficient improvement were opt for repeated TUI-BN, urethral onabotulinumtoxinA injection or transurethral external sphincter incision (TUI-ES). The current voiding status, surgical complications were evaluated.

Results: A total of 102 women with VUDS evidence of a narrow bladder neck during voiding were enrolled. The long-term success rate of the first TUI-BN was 29.4% (30/102) and increased to 66.7% (34/51) after combining TUI-BN and additional procedure. The overall long-term success rates were 74.6% in detrusor underactivity (DU), 52.0% in detrusor overactivity and low contractility, 50.0% in bladder neck obstruction (p=0.022). Spontaneous voiding was achieved in 66 (64.7%) patients, de novo urinary incontinence in 21 (20.6%), and vesicovaginal fistula in 4 (3.9%), all were repaired.

Conclusions: TUI-BN alone or in combination with additional procedure was safe, effective and durable. Patients with DU benefit most in resuming spontaneous voiding.

Introduction

Bladder neck obstruction (BNO) in men has been extensively studied, however, BNO in women is often overlooked and under-treated.[1] Previous study revealed the estimated prevalence of female BNO was between 2.7% and 29% [2–3]. The main reason leads to a large variation in the prevalence rate is the lack of standard diagnostic criteria for female BNO. [4] Clinically, the compliant of lower urinary tract symptoms (LUTS) of in female BNO are usually unreliable, which adds on challenges for physician to make accurate diagnosis of BNO.[5]

Videourodynamics study (VUDS) provides a precise diagnosis for female voiding symptoms.[6] Turner-Warwick et al. described high voiding pressure, low flow rate and non-funneling appearance of the bladder neck during voiding phase in VUDS as bladder neck dysfunction (BND).[7] However, in clinical practice, the etiology of voiding dysfunction with a narrowing bladder outlet in VUDS was hardly differentiated, such as in BND alone or in combination with a tight urethral sphincter, or with detrusor underactivity (DU).

Previous studies demonstrated transurethral bladder neck incision (TUI-BN) in women with BN obstruction and DU is effective.[8,9] However, the effectiveness in real world practice has not been determined yet. Moreover, study about repeated TUI-BN or additional procedure after the first TUI-BN to improve success rate has even scantly been reported. This study aimed to evaluate the long-term effectiveness of TUI-BN in female voiding dysfunction of different etiology and a narrow bladder neck

during voiding showing in VUDS. The effectiveness of additional procedures to TUI-BN and the predictive factors for a better treatment outcome was reported as well.

Methods

We retrospectively reviewed women who had voiding symptoms and underwent TUI-BN at least once at our institution during March 2007 till April 2019. All patients underwent VUDS before TUI-BN and after operation. Females with proven urinary tract infections, previous anti-incontinence surgery or spinal cord injury were not enrolled into the study. This study was approved by the Institutional Review Board of the Buddhist Tzu Chi Hospital (IRB: 100-06). Informed consent was waived by the Institutional Review Board of the Buddhist Tzu Chi Hospital, due to the retrospective nature of the analysis. All methods were performed in accordance with the relevant guidelines and regulations.

VUDS was performed in accordance with the recommendations of the International Continence Society.[10] A multichannel urodynamic system (Life-Tech Inc., Stafford, TX, USA) and a C-arm fluoroscope (Toshiba, Tokyo, Japan) were used. VUDS was repeated at least twice to obtain a reproducible pressure flow trace. The first sensation of filling (FSF), full sensation (FS), cystometric bladder capacity (CBC), bladder compliance, maximum flow rate (Qmax), detrusor pressure at Qmax (Pdet.Qmax), post-void residual volume (PVR), sphincter electromyography activity (EMG), voided volume (Vol), bladder outlet obstruction index (BOOI, defined as Pdet.Qmax - [2 × Qmax]), bladder contractility index (BCI, defined as BCI = Pdet Qmax + 5 Qmax), voiding efficiency (VE, defined as voided Vol / bladder capacity x 100%) and corrected maximum flow rate (cQmax, defined as $Qmax/Vol^{1/2}$) were documented. During VUDS, voiding cystourethrography was carried out using a C-arm fluoroscope positioned 45 degrees from the buttocks so that the urethra could be lengthened, and the bladder neck, urethral sphincter, and distal urethra could be clearly seen.

Patients with severe difficulty in urination, straining to voiding, large PVR, and a narrow bladder neck observed during voiding phase in VUDS, were initially treated with alpha-blockers for at least three months. If LUTS were refractory to medication, TUI-BN was advised. The surgical procedure of TUI-BN has been reported in previous study.[8] If patients still had dysuria, straining while voiding, large PVR or VE less than 25% after the initial TUI-BN, post-operative VUDS was performed. Consecutive TUI-BN, transurethral external sphincter incision (TUI-ES) or urethral sphincter onabotulinumtoxin A injection would be advised according to the findings in the second VUDS. Patients with neurological deficit such as history of cerebrovascular accident, Parkinsonism, myelomeningocele, poliomyelitis, radical hysterectomy, or spine surgery were categorized as neurologic bladder. Patients without any neurological deficit were grouped into non-neurogenic bladder. The current voiding status was collected through direct interview by the same research assistant. The surgical complications such as *de novo* incontinence and vesicovaginal fistula, and additional surgical procedures for complications such as suburethral sling implantation and urethral platelet-rich plasma (PRP) injection were documented.

The descriptions and terminology for urodynamic parameters were in accordance with the recommendations of International Continence Society[11]. We defined an improvement of VE by ≥ 50% after TUI-BN with or without additional procedure as surgical success. The parameters between success and fail group were compared using chi-square test for categorical variables and Wilcoxon rank-sum test for continuous variables. The demographics and VUDS parameters were analyzed using univariate and multivariate logistic regression to clarify the predictive factors and the discriminatory capacity was investigated using an area under the curve (AUC) analysis. A p-value <0.05 was considered as statistically significant.

Results

The age of patients ranged from 18 to 88 years old (mean 61.4 ± 17.4). Among the 102 patients, 64 (62.7%) had successful outcome and 38 (37.3%) failed the treatment in long-term follow-up. The baseline VUDS identified detrusor underactivity (DU) in 59 patents (57.8%), detrusor overactivity and low contractility (DOLC) in 23 (22.5%), hypersensitive bladder (HSB) in 9 (8.8%), and bladder neck obstruction (BNO) in 4 (3.9%). Among the patients 44/59 (74.6%) with DU, 13/25 (52.0%) with DOLC, 2/4 (50.0%) with BNO, 2/10 (20.0%) with HSB, and 3/4 (75.0%) with stable bladder were successful (p = 0.022). The success rate of DU patient after the first TUI-BN was 30.5% (18 out of 59), and the success rate increased to 76.5% (26 out of 34) in patients who received TUI-BN and additional procedure. Patients with neurogenic bladder has a higher success rate (73.1%, 38 out of 52) in comparison with non-neurogenic bladder (52%, 26 out of 50) (p = 0.028).

The baseline VUDS parameters in the success group were lower in Qmax, Vol, cQmax, BCI and VE, but higher in PVR (p < 0.05). (Table1) Significant improvement of the VUDS parameters were noted after surgery in Qmax (5.16 ± 8.53 ml/s), Vol. (93.9 ± 169.3 ml), PVR (171.2 ± 239.4 ml), cQmax (0.32 ± 0.55), BCI (17.7 ± 49.3), and VE (0.33 ± 0.42) (p < 0.001). (Table 2) Among the 102 patients, 51 underwent TUI-BN alone, 51 patients received TUI-BN and followed by additional procedures, including repeated TUI-BN in 14; TUI-BN and urethral Botox injection in 13; urethral Botox injection alone in 18; TUI-BN and urethral Botox injection and TUI-ES in 3; urethral Botox injection and TUI-ES in 2, and TUI-ES alone in 1.

Table 1
The baseline videourodynamic parameters and diagnosis of patients among success and failed groups

Parameters	Total (n=102)	Fail (n=38)	Success (n=64)	p
Age (years)	61.17±16.29	59.37±16.17	62.23±16.40	0.393
FSF (ml)	166.84±80.50	149.42±79.92	176.79±79.74	0.104
FS (ml)	256.72±107.36	230.17±105.67	271.89±106.18	0.063
CBC (ml)	423.95±199.19	381.30±188.09	449.00±202.70	0.101
Pdet.Qmax (cmH2O)	17.81±24.20	23.06±22.55	14.81±24.77	0.103
Qmax (ml/s)	3.71±4.67	5.54±4.74	2.63±4.31	0.002
Vol (ml)	80.93±113.65	139.66±136.75	46.06±80.05	<0.001
PVR (ml)	339.48±202.92	242.63±168.05	396.98±201.03	<0.001
Compliance	64.69±71.90	76.92±99.33	57.69±49.65	0.202
cQmax	0.20±0.26	0.31±0.29	0.13±0.21	<0.001
BOOI	10.54±24.38	12.28±22.71	9.54±25.41	0.593
BCI	35.99±36.54	50.00±36.11	27.98±34.57	0.003
Pves (cmH2O)	64.31±44.05	59.35±46.00	67.07±43.06	0.416
Pabd (cmH2O)	43.91±52.74	33.03±52.97	50.13±52.00	0.121
VE	0.22±0.28	0.39±0.33	0.11±0.17	<0.001
VUDS Diagnosis				0.022
Stable bladder	4 (3.92)	1 (2.63)	3 (4.69)	
BND	4 (3.92)	2 (5.26)	2 (3.13)	
DU	59 (57.84)	15 (39.47)	44 (68.75)	
DOLC	25 (24.50)	12 (31.58)	13 (20.31)	
HSB	10 (9.80)	8 (21.05)	2 (3.13)	

Data were expressed as mean ± standard deviation or number (percentage), BND: bladder neck dysfunction; DU: detrusor underactivity; DOLC: Detrusor overactivity and low contractility; HSB: Hypersensitive bladder; BOOI: bladder outlet obstruction index = Pdet.Qmax-2 x Qmax; BCI: bladder contractility index; CBC: cystometric bladder capacity; FS: full sensation; FSF: first sensation of filling; Pdet.Qmax: detrusor pressure at Qmax; Pves: vesicle pressure at Qmax; Pabd: abdominal pressure at Qmax; PVR: post-void residual; Qmax: maximum flow rate; Vol: voided volume; VE: voiding efficiency. $p<0.05$ considered significant difference.

Table 2
The changes of VUDS parameter after surgery

Parameters	Total (n=102)	Fail (n=38)	Success (n=64)	P=
FSF (ml)	-6.79±109.05	17.68±100.13	-25.91±113.40	0.136
FS (ml)	-2.16±141.05	25.92±125.40	-24.09±150.44	0.186
CBC (ml)	-89.30±224.01	-35.88±211.45	-121.89±226.91	0.069
Pdet.Qmax (cmH2O)	-4.32±24.98	-4.68±21.78	-4.03±27.57	0.924
Qmax (ml/s)	5.16±8.53	0.56±6.21	8.15±8.54	<0.001
Vol (ml)	93.87±169.26	-26.51±95.06	159.71±165.03	<0.001
PVR (ml)	-171.21±239.43	-0.33±181.04	-272.67±211.16	<0.001
Compliance	2.68±113.79	13.34±163.58	-5.64±50.08	0.537
cQmax	0.32±0.55	0.08±0.46	0.48±0.55	<0.001
BOOI	-16.77±33.15	-9.33±32.21	-21.45±33.24	0.138
BCI	17.71±49.32	-8.81±35.13	34.37±49.96	<0.001
Pves (cmH2O)	-4.09±50.79	-0.92±54.77	-6.63±48.18	0.685
Pabd (cmH2O)	-6.20±54.79	4.82±58.94	-13.73±51.14	0.169
VE	0.33±0.42	-0.08±0.25	0.57±0.29	<0.001

Data were expressed as mean ± standard deviation or number (percentage), BOOI: bladder outlet obstruction index = Pdet.Qmax-2 x Qmax; BCI: bladder contractility index; CBC: cystometric bladder capacity; FS: full sensation; FSF: first sensation of filling; Pdet.Qmax: detrusor pressure at Qmax; Pves: vesicle pressure at Qmax; Pabd: abdominal pressure at Qmax; PVR: post-void residual; Qmax: maximum flow rate; Vol: voided volume; VE: voiding efficiency. p<0.05 considered significant difference.

The entire *de novo* incontinence was grade 1 stress urinary incontinence and the prevalence rate was 20.6% (n= 21), and vesicovaginal fistula 3.9% (n=4). The prevalence rate of *de novo* stress urinary incontinence was 36.7% (11 out of 30) in patients with TUI-BN alone, and was 13.9% (10 out of 72) in patients received TUI-BN and additional procedure. Among the 21 patients who had postoperative urinary incontinence needed more than 1 pad/day, 12 underwent suburethral sling surgery and 2 patients underwent urethral sphincter PRP injection. Patients with vesicovaginal fistula received immediately transvaginal fistula repair during the same operation, and all were successfully treated.

The overall success rate was 62.7%, including 29.4% (30 out of 102) with the first TUI-BN alone, and additional 66.7% (34 out of 51) who had combined TUI-BN with additional procedure (p<0.001). Among 102 patients, the current voiding status was spontaneous voiding in 66 (64.7%) patients, self-voiding with occasional CIC in 21 (20.6%), CIC dependence in 12 (11.8%), and indwelling a catheter in 3 (2.9%).

A logistic regression univariate analysis showed neurogenic bladder, lower Vol, lower cQmax, higher PVR at baseline significantly predicted satisfactory surgical outcome [odds ratio (OR) = 2.51, $p = 0.029$; OR = 0.99, $p < 0.001$; OR = 0.06, $p = 0.002$; and OR = 1, $p < 0.001$, respectively]. The multivariate analysis showed only Vol and PVR were the significant predictor for surgical outcome (OR= 0.99, $p = 0.016$; and OR = 1.00, $p = 0.021$, respectively). (Table 3)The receiver operating curve analysis of baseline Vol and PVR showed the area under the curve were 0.74 (95% confidence interval= 0.63 to 0.84) and 0.72 (95% confidence interval= 0.62 to 0.82), respectively. (Figure 1) The optimal cutoff value of Vol. was 38ml, with acceptable specificity 74.0% and sensitivity 73.0%; PVR was 335ml, with specificity 74.0% and sensitivity 59.0%. Age, underline comorbidity such as coronary disease, congestive heart failure, diabetes mellitus, hypertension and cerebrovascular accident showed no significant correlation to surgical outcome.

Table 3
The univariate and multivariate analysis of predictor factors associated with success rate

	Univariate		Multivariate	
Parameters	**OR (95% CI)**	**p**	**OR (95% CI)**	**p**
Age	1.01 (0.99 to 1.04)	0.390		
CAD	0.32 (0.07 to 1.44)	0.140		
CHF	1.19 (0.10 to 13.62)	0.887		
DM	1.52 (0.49 to 4.72)	0.466		
HTN	1.58 (0.68 to 3.68)	0.288		
CVA	0.88 (0.23 to 3.34)	0.850		
Neurogenic bladder	2.51 (1.10 to 5.73)	0.029	0.99 (0.36 to 2.73)	0.978
FSF	1.00 (1.00 to 1.01)	0.108		
FS	1.00 (1.00 to 1.01)	0.066		
CBC	1.00 (1.00 to 1.00)	0.106		
P_{det}	0.99 (0.97 to 1.00)	0.114		
Vol	0.99 (0.99 to 1.00)	<0.001	0.99 (0.99 to 1.00)	0.016
PVR	1.00 (1.00 to 1.01)	<0.001	1.00 (1.00 to 1.01)	0.021
Compliance	1.00 (0.99 to 1.00)	0.212		
cQmax	0.06 (0.01 to 0.35)	0.002	1.60 (0.14 to 18.93)	0.709
BOOI	1.00 (0.98 to 1.01)	0.591		
P_{ves}	1.00 (0.99 to 1.01)	0.413		

CAD: coronary artery disease; CHF: congestive heart failure; DM: Diabetes Mellitus; HTN: hypertension; CVA: cerebrovascular accident; FS: full sensation; FSF: first sensation of filling; CBC: cystometric bladder capacity; $P_{det.Qmax}$: detrusor pressure at Qmax; Vol: voided volume; PVR: post-void residual; Qmax: maximum flow rate; cQmax: corrected maximum flow rate; P_{ves}: vesicle pressure at Qmax; P_{abd}: abdominal pressure at Qmax; BOOI: bladder outlet obstruction index = $P_{det.Qmax}$-2 x Qmax; BCI: bladder contractility index; VE: voiding efficiency; DOLC: detrusor overactivity and low contractility. $p<0.05$ considered significant difference.

Receiver operating characteristic curve of baseline post-void residual urine (PVR) and voided volume (Vol.) for predicting satisfactory surgical outcome after transurethral incision of bladder neck. The area under the curve (AUC) was 0.72 (95% confidence interval= 0.62 to 0.82) and 0.74 (95% confidence interval= 0.63 to 0.84) respectively. The optimal cutoff value of PVR was 335, with specificity 74.0% and sensitivity 59.0% and of Vol. was 38ml, with acceptable specificity 74.0% and sensitivity 73.0%.

	Univariate	Multivariate
P_{abd}	1.01 (1.00 to 1.02)	0.125
DOLC	0.49 (0.20 to 1.19)	0.116

CAD: coronary artery disease; CHF: congestive heart failure; DM: Diabetes Mellitus; HTN: hypertension; CVA: cerebrovascular accident; FS: full sensation; FSF: first sensation of filling; CBC: cystometric bladder capacity; $P_{det.Qmax}$: detrusor pressure at Qmax; Vol: voided volume; PVR: post-void residual; Qmax: maximum flow rate; cQmax: corrected maximum flow rate; P_{ves}: vesicle pressure at Qmax; P_{abd}: abdominal pressure at Qmax; BOOI: bladder outlet obstruction index = $P_{det.Qmax}$-2 x Qmax; BCI: bladder contractility index; VE: voiding efficiency; DOLC: detrusor overactivity and low contractility. $p<0.05$ considered significant difference.

Receiver operating characteristic curve of baseline post-void residual urine (PVR) and voided volume (Vol.) for predicting satisfactory surgical outcome after transurethral incision of bladder neck. The area under the curve (AUC) was 0.72 (95% confidence interval= 0.62 to 0.82) and 0.74 (95% confidence interval= 0.63 to 0.84) respectively. The optimal cutoff value of PVR was 335, with specificity 74.0% and sensitivity 59.0% and of Vol. was 38ml, with acceptable specificity 74.0% and sensitivity 73.0%.

Discussion

Female voiding dysfunction is frequently encountered in urological practice due to neurogenic or non-neurogenic etiologies, including DU, BNO, or unknown causes.[12] Although CIC is the standard treatment option, patients usually wish to void spontaneously without the need of a catheter, in order to have a better life quality. This study demonstrated TUI-BN alone or in combination with additional procedure was safe, effective, and long-term durable in 62.7% of women. Patients with DU benefit most in resuming spontaneous voiding.

DU exists among elderly resulting in chronic urinary retention, recurrent urinary tract infection, deteriorating of renal function and long-term catheterization, which affected life quality. Up to now, there is limited effective pharmacotherapy and lack of consensus in treating DU patients.[13] TUI-BN has a promising high success rate 74.6% to resume spontaneous voiding in DU patients and our promising effect was similar to previous studies.[9,14] An adequate incision of the bladder neck smooth muscle until the serosa is crucial for a successful surgical outcome.

A wide-open bladder neck under cystoscopy; and funnel shape of the bladder neck opening during voiding phase effectively reduces the resistance of bladder outlet. In the premise of adequate abdominal pressure, TUI-BN may facilitate spontaneous voiding in DU patients by abdominal straining resulting in increased VE and reduced PVR. Interestingly, this study revealed a dramatic improvement in Qmax by 413.3%, Vol. by 346.7%, cQmax by 369.2%, BCI by 122.8%, and PVR by 68.7% in the success group after treatment. TUI-BN alone or combining additional surgery provided a promising surgical outcome in

patients with DU. Therefore, TUI-BN might be considered as a standard therapy for DU patient if medical treatment failed and patients desired a spontaneous voiding without CIC.

Based on the analysis of urodynamic parameters, the study revealed a higher PVR and a lower voided volume at baseline are the predictive factors for a successful surgical outcome. Bladder neck plays a crucial role in voiding phase. High sympathetic tone of the bladder neck might lead to negative feedback that inhibited the detrusor contractility during voiding phase. [15] In this study, the BCI improved by 122.8% once TUI-BN was performed. The previous study revealed an open bladder neck on voiding cystourethrography is the only predictive factor for successful urethral sphincter onabotulinumtoxinA injection in patients with voiding dysfunction regardless neurogenic or non-neurogenic based.[16,17] Once the bladder neck was opened widely by TUI-BN with or without additional TUI-BN, TUI-ES, or urethral sphincter onabotulinumtoxin A injection could subsequently provide a promising surgical outcome with additional success rate of 64.7% in those who failed the first TUI-BN.

A closed bladder neck and urethral opening were usually noted during voiding phase in DU patient with or without neuropathy in VUDS. It is a challenge to distinguish between the association of inadequate detrusor contractility, bladder neck dysfunction or tight urethral external sphincter especially in DU patients during VUDS. Sympathetic nerve mediated by adrenergic alpha-receptors extends from the bladder neck and prostate to the external urethral sphincter in male.[18] Pudendal nerve stimulation evoked somatic responses in the external urethral sphincter and increased bladder neck pressure.[19] In this study, the success rate for TUI-BN alone particularly in DU patients was only 30.5%, however, the success rate can be achieved to 76.5% with the combination of additional surgery such as repeat TUI-BN, urethral sphincter onabotulinumtoxin A injection or TUI-ES. Therefore, in patients who failed the initial TUI-BN, a precise post-operative VUDS was mandatory and additional surgery was essential in order to resume spontaneous voiding.

In this study, 90.4% of patients with neurogenic bladder had the diagnosis of DU. Population with neurogenic bladder were younger in age, mostly due to post-pelvic surgery. Therefore, the patients usually had a stronger abdominal pressure while voiding. The reduction of bladder neck resistance by TUI-BN and additional surgery enables spontaneous voiding in neurogenic bladder patients, with VE improved up to 50%. On the other hand, most of the patients with non-neurogenic bladder were lack of abdominal straining ability, as they were frail and associated with multiple underline comorbidity

Patients with hypersensitive bladder had the lowest success rate of 22.2%. In previous study, bladder pain causing bladder outlet dysfunction, and one third of the patients was found to have functional obstruction at the external sphincter. Chronic inflammation of the bladder might result in external sphincter hyperactivity while voiding.[20] Visceral pain syndromes might associate with central and peripheral sensitization and lowering of nociceptive threshold, resulting in neuropathic upregulation, hypersensitivity, allodynia and dysfunctional voiding.[21] Increased pudendal afferent activity through the guarding reflex of the external urethral sphincter, and thus inhibited the efficiency of bladder contractility.[22] The ongoing chronic inflammation sustained the external sphincter spasticity addition to

inhibition of bladder contractility, lead to less satisfactory surgical outcome despite undergoing TUI-BN or additional surgery.

The adverse event of TUI-BN and additional surgery was limited and confined to certain population. Among the four patients who developed vesicovaginal fistula, 3 of the patients underwent TUI-BN twice and one of them underwent additional TUI-ES twice. Interestingly, all of them associated with *de novo* incontinence and underwent suburethral sling surgery latterly and 2 of them underwent additional urethral sphincter PRP injection. Autologous PRP is rich in growth factors and cytokines, which regulate tissue reconstruction that augments wound healing, speed the recovery from muscle and joint injuries, and enhance recovery after surgical repair.[23] PRP was injected at the urethral external sphincter in order to increase urethral resistance. [24] Currently, three patients resumed spontaneous voiding and another one was under self-voiding and CISC. The confined patients underwent multiple repeated surgeries and complication recovery surgery mainly due to unhealthy localized tissue and repeated surgeries caused tissue adhesion. Besides, 12 patients were reported underwent suburethral sling surgery due to *de novo* incontinence after TUI-BN. All of them had recovered from stress urinary incontinence, 8 patients were under self-voiding, 3 patients under CISC with self-voiding, and another patient under CISC.

The limitation of this study is by its retrospective designs and single-center experience. A prospective study should be designed to validate the effectiveness of TUI-BN in female with voiding dysfunction and a tight bladder neck.

Conclusions

TUI-BN alone or in combination with additional procedure was safe, effective and durable. Patients with DU have the best success rate in resuming spontaneous voiding after treatment. The lower voided volume and higher post-void residual volume showed significant association for likelihood for treatment success.

Declarations

IRB: This study was approved by the Institutional Review Board of the Buddhist Tzu Chi Hospital (IRB: 100-06). Informed consent was waived by the Institutional Review Board of the Buddhist Tzu Chi Hospital, due to the retrospective nature of the analysis. All methods were performed in accordance with the relevant guidelines and regulations.

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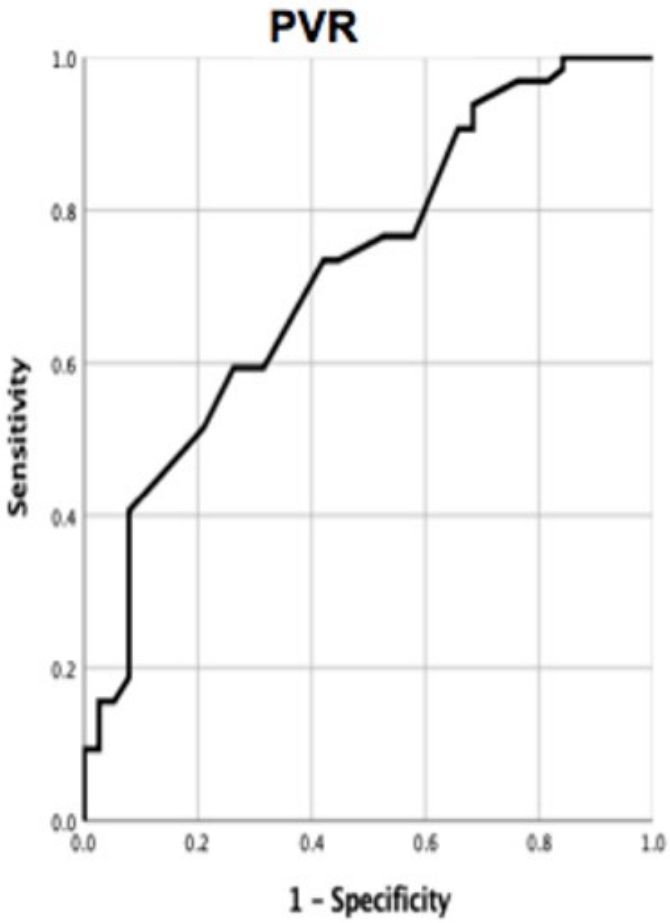
References

1. Choi, Y. S. *et al.* Analysis of female voiding dysfunction: a prospective, multi-center study. *Int Urol Nephron*, **45**, 989–994 (2013).

2. Gordon, D. & Groutz, A. Evaluation of female lower urinary tract symptoms: overview and update. *Curr Opin Obstet Gynecol*, **13**, 521–527 (2001).
3. Groutz, A. & Blaivas, J. G. Non-neurogenic female voiding dysfunction. *Curr Opin Urol*, **12**, 311–316 (2002).
4. Patel, R. & Nitti, V. Bladder outlet obstruction in women: prevalence, recognition, and management. *Curr Urol Rep*, **2**, 379–387 (2001).
5. Kuo, H. C. Clinical symptoms are not reliable in the diagnosis of lower urinary tract dysfunction in women. *J Formos Med Assoc*, **111**, 386–391 (2012).
6. Kuo, H. C. Videourodynamic characteristics and lower urinary tract symptoms of female bladder outlet obstruction. *Urology*, **66**, 1005–1009 (2005).
7. Turner-Warwick, R. *et al.* A urodynamic view of the clinical problems associated with bladder neck dysfunction and its treatment by endoscopic incision and trans-trigonal posterior prostatectomy. *Br J Urol*, **45**, 44–59 (1973).
8. Peng, C. H. & Kuo, H. C. Transurethral incision of bladder neck in treatment of bladder neck obstruction in women. *Urology*, **65**, 275–278 (2005).
9. Jhang, J. F., Jiang, Y. H., Lee, C. H. & Kuo, H. C. Long-term follow up and predictive factors for successful outcome of transurethral incision of the bladder neck in women with detrusor underactivity. *J Formosan Med Assoc*, **115**, 807–813 (2016).
10. Game, A. *et al.* International Continence Society Guidelines on urodynamic equipment performance. *Neurourol Urodyn*, **33**, 370–379 (2014).
11. Haylen, B. T. *et al.* An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. *Int Urogynecol J*, **21**, 5–26 (2010).
12. Hsiao, S. M., Lin, H. H. & Kuo, H. C. Videourodynamic studies of women with voiding dysfunction. *Sci Rep*, **7**, 6845 (2017).
13. Juszczak, K. & Drewa, T. Pharmacotherapy in detrusor underactivity: A new challenge for urologists and pharmacologists (from lab to clinic). *Pharmacol Rep*, **68**, 703–706 (2016).
14. Jhang, J. F., Jiang, Y. H. & Kuo, H. C. Transurethral incision of the bladder neck improves voiding efficiency in female patients with detrusor underactivity. *Int Urogynecol J*, **25**, 671–676 (2014).
15. Yoshimura, N. & de Groat, W. C. Neural control of the lower urinary tract. *Int J Urol*, **4**, 111–125 (1997).
16. Jiang, Y. H., Chen, S. F., Jhang, J. F. & Kuo, H. C. Therapeutic effect of urethral sphincter onabotulinumtoxinA injection for urethral sphincter hyperactivity. *Neurourol Urodyn*, **37**, 2651–2657 (2018).
17. Jiang, Y. H., Jhang, J. F., Chen, S. F. & Kuo, H. C. Videourodynamic factors predictive of successful onabotulinumtoxinA urethral sphincter injection for neurogenic or non-neurogenic detrusor underactivity. *Low Urin Tract Symptoms*, **11**, 66–71 (2019).

18. Elbadawi, A. & Schenk, E. A. A new theory of the innervation of bladder musculature. Part 4. Innervation of the urethrovesical junction and external urethral sphincter. *J Urol*, **111**, 613–615 (1974).
19. Reitz, A. *et al.* Afferent fibers of the pudendal nerve modulate sympathetic neurons controlling the bladder neck. *Neurourol Urodyn*, **22**, 597–601 (2003).
20. Kuo, Y. C. & Kuo, H. C. Adverse events of intravesical OnabotulinumtoxinA injection between patients with overactive bladder and interstitial cystitis-different mechanisms of action of botox on bladder dysfunction? *Toxins*, **8**, 75 (2016).
21. Faubion, S. S., Shuster, L. T. & Bharucha, A. E. Recognition and management of nonrelaxing pelvic floor dysfunction. Mayo Clin Proc. 87,187–193(2012)
22. Park, J. M., Bloom, D. A. & McGuire, E. J. The guarding reflex revisited. *Br J Urol*, **80**, 940–945 (1997).
23. Eppley, B. L., Woodell, J. E. & Higgins, J. Platelet quantification and growth factor analysis from platelet-rich plasma: Implications for wound healing. *Plast Reconstr Surg*, **114**, 1502–1508 (2014).
24. Jiang, Y. H., Lee, P. J. & Kuo, H. C. Therapeutic efficacy of urethral sphincter injections of platelet-rich plasma for the treatment of stress urinary incontinence due to intrinsic sphincter deficiency - a proof of concept clinical trial.*Int Neurourol J* https://doi.org/10.5213/inj.2040272.136 (2021).

Figures



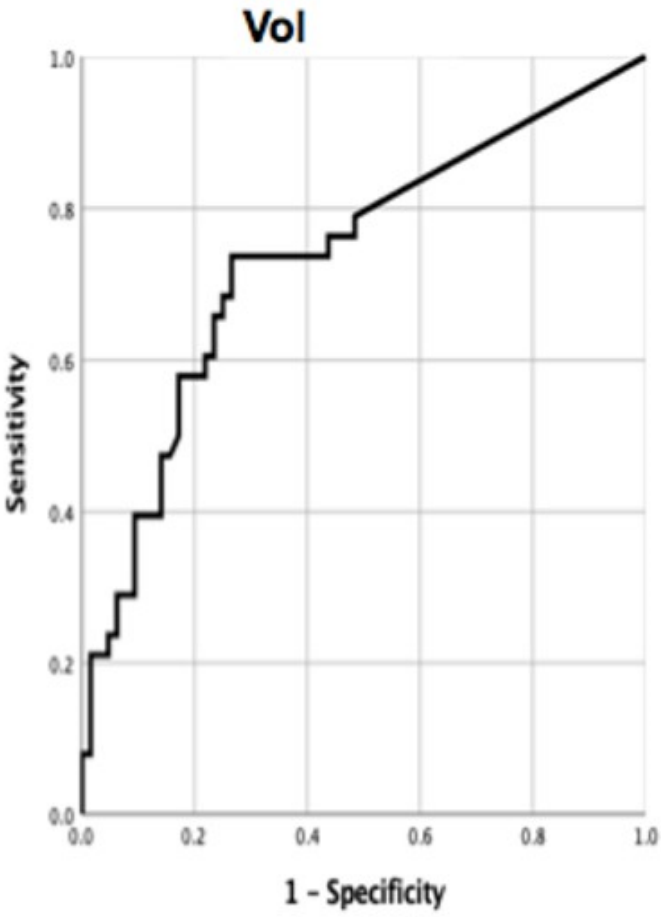


Figure 1

Receiver operating characteristic curve of baseline post-void residual urine (PVR) and voided volume (Vol.) for predicting satisfactory surgical outcome after transurethral incision of bladder neck. The area under the curve (AUC) was 0.72 (95% confidence interval= 0.62 to 0.82) and 0.74 (95% confidence interval= 0.63 to 0.84) respectively. The optimal cutoff value of PVR was 335, with specificity 74.0% and sensitivity 59.0% and of Vol. was 38ml, with acceptable specificity 74.0% and sensitivity 73.0%.