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Efficacy and Safety of Transurethral Enucleation with Bipolar Energy for Treatment of Benign Prostatic Hyperplasia: Does Prostate Volume Matter?

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Background: We evaluated the association of prostate volume (PV) with the efficacy and safety of transurethral enucleation with bipolar energy (TUEB) for treatment of benign prostatic hyperplasia (BPH).

Methods: We retrospectively evaluated data from 180 patients with symptomatic BPH who underwent TUEB between 2008 and 2015. Efficacy was assessed by perioperative changes in international prostate symptom score (IPSS), Quality of Life Score (QOLS), maximum flow rate on uroflowmetry (Qmax), and serum prostate-specific antigen level (PSA), which were recorded at 3 months postoperatively. Safety was assessed by perioperative incidence of adverse events (AEs). AEs were recorded up to 2 years after surgery. Patients were divided into two groups based on PV as the standard group (SG; PV < 80 mL) and large group (LG; PV ≥ 80 mL).

Results: A total of 132 (73%) patients were grouped as the SG, and 48 (27%) were grouped as the LG. No significant differences between the groups were observed in the preoperative variables age, IPSS, and QOLS. However, the LG had a significantly larger PV and higher serum PSA levels. Analysis of surgical outcomes revealed that postoperative changes in IPSS, QOLS, Qmax, serum PSA, serum sodium, and hemoglobin levels did not differ significantly between groups. However, LG had a significantly longer operative time and heavier specimen weight. The rates of early complications, including hyponatremia and blood transfusion, and late complications after surgery did not differ between the groups.

Conclusion: The present findings suggest that TUEB is safe and effective for treatment of BPH, regardless of PV. (J Nippon Med Sch 2022; 89: 436–442)

Key words: transurethral enucleation, benign prostatic hyperplasia, transurethral resection, efficacy

Introduction

Benign prostate hyperplasia (BPH) is the most common cause of lower urinary tract symptoms in older men[1]. Current indications for BPH-related surgery include unimproved lower urinary tract symptoms (LUTS) despite medical therapy and complicated conditions such as acute urinary retention, recurrent or persistent urinary tract infection, bladder stones, and refractory gross hematuria[2]. Invasive surgical therapies, such as transurethral resection of the prostate (TURP) and simple open prostatectomy (OP), are the standard surgical interventions for BPH[3,4]. However, these invasive procedures are associated with considerable perioperative morbidity, including postoperative bleeding, TUR syndrome, and urethral stricture[4]. Other disadvantages of TURP are resection without enucleation, which causes bleeding and requires

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the use of hypotonic irrigation fluid, which may lead to hyponatremia.

Various surgical techniques have been introduced to address these problems. In 1986, transurethral enucleation (TUE), the first endoscopic enucleation technique, was reported[5]. However, owing to the absence of electric cauterization, bleeding cannot be stopped during enucleation. In 1990, endoscopic vaporization of the prostate (EVP) with a neodymium YAG laser was first reported. Later, EVP with other types of lasers was introduced. The efficacy and safety of the laser were found to be comparable to those of TURP[6]. However, because the EVP procedure did not include enucleation, EVP methods remove a smaller amount of apical prostate tissue, to prevent sphincter injury[6]. Holmium laser enucleation of the prostate (HoLEP) was first reported in 1995[7] and results in lower morbidity, shorter hospital stays, and good efficacy regardless of prostate size. Although the system is expensive and requires a morcellator, it is safe and effective; HoLEP has thus become the new standard surgical treatment for BPH.

Transurethral enucleation with bipolar energy (TUEB) was first reported in 2007. This procedure was developed by the Olympus Corporation (Tokyo, Japan) and uses a transurethral resection in saline (TURis) system, TUEB loop, and a morcellator[8]. An improved TUEB method without morcellation, which overcomes the disadvantages of TURP, HoLEP, and TUEB with morcellation, was reported 10 years later. TUEB without morcellation has efficacy equivalent to that of TURis but with less bleeding and shorter hospital stays[9]. However, the efficacy and safety of TUEB in relation to prostate volume are unclear. In this study, we evaluated whether prostate volume was associated with the efficacy and safety of TUEB for treating BPH.

Materials and Methods

After receiving institutional review board approval, we reviewed the records of 180 consecutive patients who underwent TUEB between December 2008 and December 2015 at our center. All patients presented with LUTS or urinary retention, which persisted despite comprehensive medical treatment. Patients with a history of prostate cancer, neurogenic bladder, preoperative urethral stricture, or bladder cancer were excluded. All surgically resected specimens were subjected to pathological examination. Informed consent was obtained from all patients before the surgical intervention. All procedures were performed by the same surgeon.

Clinical Data

Patient demographic and clinical data were recorded, namely, international prostate symptom score (IPSS); Quality of Life Score (QOLS); maximum flow rate on uroflowmetry (Qmax); hemoglobin (Hb), serum prostate-specific antigen (PSA), and serum sodium levels; transrectal prostate ultrasonography (TRUS) findings; surgical time; enucleated tissue weight; duration of urethral catheter placement; and perioperative complications. IPSS, QOLS, Qmax, and PSA levels at postoperative 2 months were compared with preoperative values to assess procedural efficacy. Data for postoperative hemoglobin (Hb) and serum sodium levels were compared with preoperative values to assess procedure safety. Perioperative adverse events (AE) were recorded for 2 years after surgery. Urinary incontinence after TUEB was defined as involuntary leakage of urine that required the use of more than one pad and one safety pad is allowed. Patients were classified by prostate volume (PV), as measured by TRUS, as the standard group (SG; PV < 80 mL) and large group (LG; PV ≥ 80 mL).

Technique and Equipment

The equipment used to perform the TUEB procedure included a bipolar electrosurgical system (Olympus SurgMaster; Olympus Europa Holding GmbH, Hamburg, Germany), TURis system, TUEB loop (consisting of a spatula for blunt tissue enucleation and a standard wire loop for bipolar hemostasis), and standard wire loop for tissue resection (**Fig. 1**).

Before resection, intraoperative cystoscopy was performed to assess the pattern of prostate enlargement and rule out any concomitant urethral and bladder disease. A schematic of the three-lobe TUEB procedure with accompanying intraoperative photographs is shown in **Figure 1**. First, resection was performed at the 5 o'clock and 7 o'clock positions. Adenomatous tissue from the 11 o'clock to the 1 o'clock position was then resected until the depth of the surgical capsule. Next, enucleation of the median lobe was performed, and an all-around, full-thickness, mucosal incision was made proximal to the external sphincter complex, starting from a point just proximal to the verumontanum. Then, each lateral lobe was enucleated from the distal side toward the bladder neck. Instead of releasing the vascularized lobes into the bladder, they were left hanging in the bladder neck. Subsequently, each enucleated lobe was fragmented with the conventional electrocautery wire loop, starting from the top and moving toward the floor of the fossa. The prostate chips were evacuated, and adequate hemostasis was

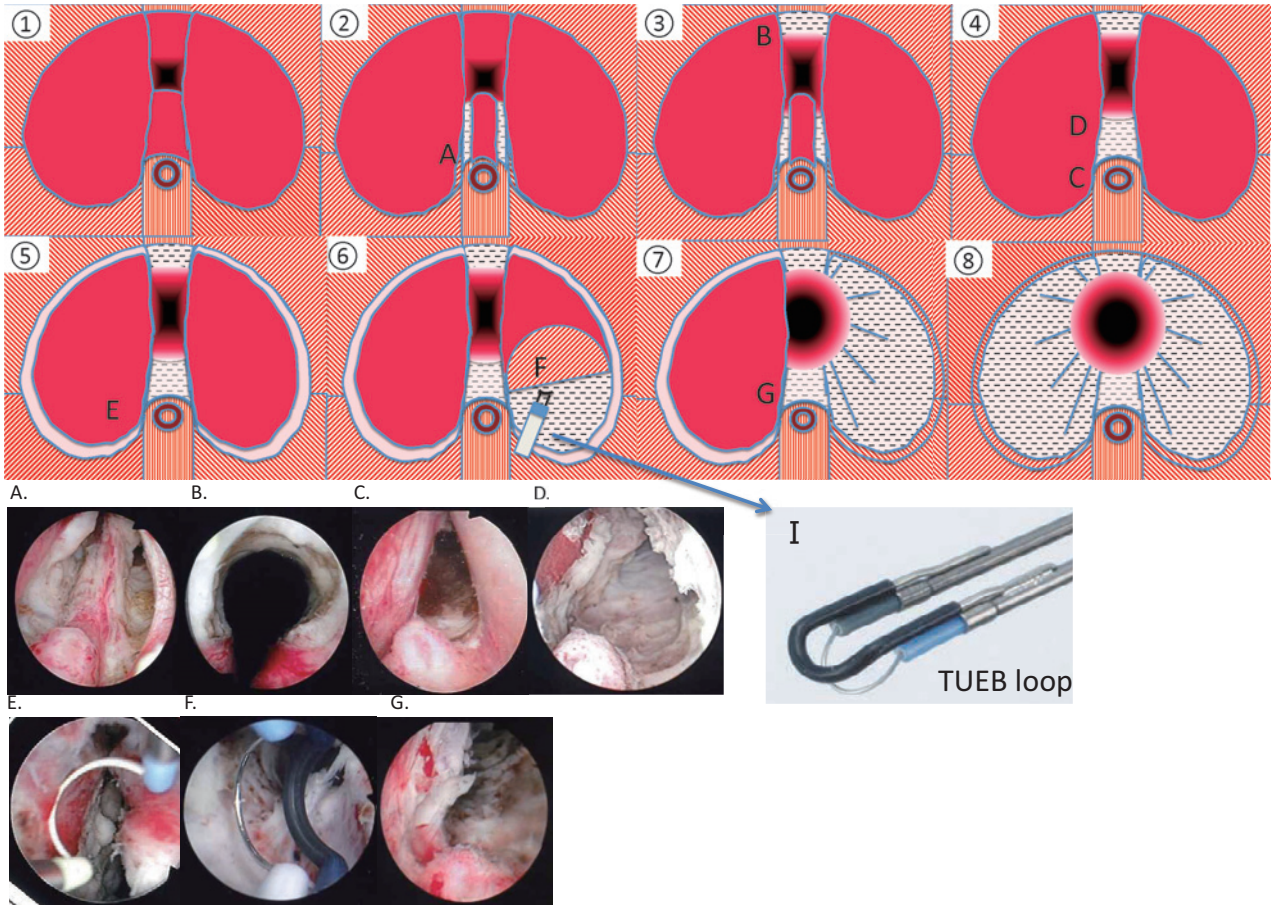


Fig. 1 The TUEB loop consists of a spatula for tissue enucleation and a standard wire loop for bipolar hemostasis (I). Schematic diagram of the TUEB procedure: three-lobe technique. ① to ⑧ shows the successive components of the technique. The observation was performed before resection (①). First, resection was performed at the 5 o'clock and 7 o'clock positions (②). (A) At the 6 o'clock position around the verumontanum. Thereafter, adenomatous tissue at the 11 o'clock to 1 o'clock position was resected to the depth of the surgical capsule (③). (B) At the 12 o'clock position around the sphincter. Next, enucleation of the median lobe was performed (④). (C) At the 6 o'clock position of the urethra around the verumontanum, and (D) At the 6 o'clock position of the urethra after mid-lobe enucleation. A full circumferential mucosal incision was then made starting from just proximal to the verumontanum (⑤). (E) The urethra while the right lobe mucosal incision was made. Subsequently, each lateral lobe was enucleated from the distal side toward the bladder neck (⑥, ⑦). (F) The urethra during left lobe enucleation. (G) At the 6 o'clock position of the urethra around the verumontanum after completion of right lobe enucleation. Instead of releasing the vascularized lobes into the bladder, they were left hanging on the bladder neck. Thereafter, each enucleated lobe was fragmented from the top toward the bottom of the fossa using a conventional electrocautery wire loop. After fragmentation, the operation was complete (⑧).

achieved. Continuous postoperative saline irrigation via a urethral catheter was performed for 24 h in all cases. Catheter removal was attempted at approximately 60 h postoperatively.

Statistical Analysis

Statistical analyses were conducted using SPSS software version 20 (IBM Corp., Armonk, NY, USA). The chi-square test and Student t-test were used to compare preoperative and postoperative data as appropriate. A *P*-value of <0.05 was considered statistically significant.

Results

The demographic and clinical characteristics of the 180 patients are shown in **Table 1**. The overall median age was 70 years (range, 55-84 years). Fifteen patients (8.3%) experienced urinary retention and had a urethral catheter placed before the surgical intervention. For the remaining patients (n = 165), the preoperative mean IPSS was 20.4 ± 8.3, QOLS was 5.0 ± 1.0, Qmax was 6.6 ± 3.3 mL/s, and mean PV was 67.1 ± 29.6 mL. The mean operation time was 101.0 ± 37.4 min, and the mean retrieved volume of prostatic tissue was 35.8 ± 15.9 g. Urethral catheters were removed after a mean duration of 2.6 ± 0.4 days.

Table 1 Patient characteristics, surgical outcomes, and efficacy variables (n = 180)

	Total	SG	LG	*P*
No. of patients, n (%)	180 (100%)	132 (73.3%)	48 (26.7%)	
Age, years	70.0	69.5	71.2	0.107
Mean serum PSA level, ng/mL	6.9	5.6	10.3	0.002
Estimated prostate volume on TRUS, mL	67.1	52.9	106.2	<0.001
Preoperative catheterization	16	9	7	0.103
Baseline IPSS	20.4	20.1	21.2	0.51
Baseline QOLS	5.0	4.9	5.1	0.332
Baseline Qmax, mL/s	6.6	6.6	6.1	0.534
Surgical outcomes				
Total operative time, min	101.9	85.9	146.2	<0.001
Total specimen weight, g	35.8	26.1	62.5	<0.001
Perioperative catheterization time, day	2.6	2.6	2.6	0.958
Efficacy variables				
IPSS (total) decrease	15.8	16.1	14.8	0.408
Voiding score decrease	7.8	8.1	5.8	0.051
Storage score decrease	5.0	5.1	4.0	0.185
QOLS decrease	3.3	3.4	3.2	0.558
Qmax (mL/s) increase	11.9	10.9	15.9	0.182
PSA decrease rate (%)	89.4	89.1	89.9	0.342

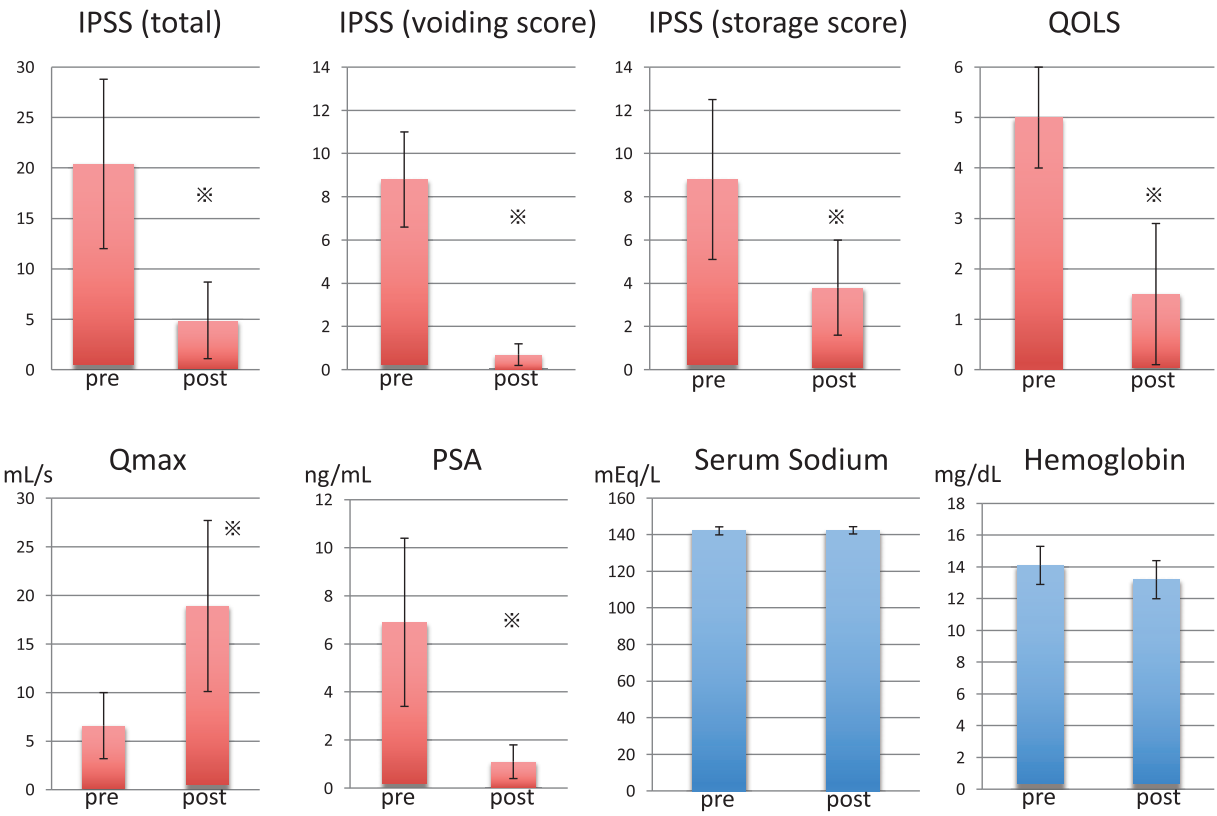
SG, standard prostate group; LG, large prostate group; PV, prostate volume; PSA, prostate-specific antigen; TRUS, transrectal ultrasonography; IPSS, international prostate symptom score; QOLS, Quality of Life Score; Qmax, maximum urinary flow rate.

The SG and LG comprised 132 (73%) and 48 patients (27%), respectively. The mean PV in each group was 52.9 ± 13.7 mL and 106.2 ± 26.6 mL, respectively. The mean operation time was significantly longer in the LG than in the SG (146.2 ± 34.0 min vs. 85.9 ± 22.9 min, respectively; $P < 0.001$).

Data for efficacy variables are shown in **Table 1** and **Figure 2**. The mean postoperative decrease was 15.8 ± 9.0 for IPSS and 3.3 ± 1.6 for QOLS. The mean increase in Qmax was 11.9 ± 10.2 mL/s. Postoperative serum PSA decreased by an average of 89.4%. All efficacy variables, including voiding and storage symptom sub-scores, revealed significant improvement as compared with the baseline ($P < 0.001$) (**Fig. 2**).

Data for safety variables, including perioperative complications, are shown in **Table 2**. There were no conversions to open surgery or TURP. The mean preoperative and postoperative Hb levels were 14.1 ± 1.2 and 13.2 ± 1.2 mg/dL, respectively, with no significant difference. The mean preoperative and postoperative serum sodium levels were 140.5 and 141.2 mEq/dL, respectively, with no significant difference. As for perioperative complications, no patient received a blood transfusion or developed hyponatremia. Five patients (2.7%) experienced clot retention, one (0.5%) of whom required reoperation and thus underwent transurethral coagulation a few hours after the index procedure. The other four (2.2%) developed clot retention after discharge. All improved with urethral catheter irrigation. All five clot retention cases occurred in the first half of our series. Only one patient (0.7%) developed urinary retention due to heavy alcohol intake soon after discharge. Three patients (1.7%) experienced urinary stress incontinence after catheter removal, but all became pad-free within 3 months after surgery. Ten patients (5.4%) developed urethral stricture; nine were managed with urethral bougie dilatation, and one underwent transurethral incision. All perioperative complications occurred within 6 months after surgery. Twelve patients (6.6%) had an incidental carcinoma with no signs of progression during follow-up.

Comparing the SG and LG, on preoperative characteristics (**Table 1**), serum PSA (5.8 ± 4.7 ng/dL vs. 10.3 ± 10.1 ng/dL, respectively; $P = 0.002$) and estimated PV by TRUS (52.9 ± 13.7 mL vs. 106.2 ± 26.6 mL, respectively; $P < 0.001$) were significantly higher in the LG. As for surgical outcomes, total operative time (85.9 ± 22.9 min vs. 146.2 ± 34.0 min, respectively; $P < 0.001$) was significantly longer and total specimen weight (26.1 ± 3.8 g vs. 62.5 ± 21.4 g, respectively; $P < 0.001$) was significantly heavier in the LG. No significant differences were ob-



IPSS, international prostate symptom score; QOLS, quality of life score;
Qmax, maximum flow rate flow rate on uroflowmetry ; PSA, prostate-specific antigen.

Fig. 2 Preoperative and postoperative characteristics of the patients. Efficacy variables are shown as red bars and safety variables as blue bars. Significant differences (P<0.001) are indicated by asterisks (*).

Table 2 Safety variables and perioperative complications (n = 180)

	Total	SG	LG	*P*
Perioperative complications				
Early events	**9 (5.0%)**	**8 (6.1%)**	**1 (2.1%)**	**0.232**
Postoperative hemorrhage				
With reoperation	1 (0.6%)	1 (0.8%)	0	0.653
Without reoperation	5 (2.8%)	5 (3.8%)	0	0.110
Serum sodium decrease (mEq/L)	0.8	5.1	2.7	0.295
Hemoglobin decrease (g/dL)	0.9	1.4	1.0	0.423
Acute urinary retention	1 (0.6%)	1 (0.8%)	0	0.653
Acute urinary tract infection	2 (1.1%)	1 (0.8%)	1 (2.1%)	0.881
Blood transfusion	0	0	0	0.900
Late events	**13 (7.7%)**	**11 (8.3%)**	**2 (4.2%)**	**0.090**
Urethral stenosis				
With operation	1 (0.5%)	1 (0.8%)	0	0.810
Without operation	9 (4.9%)	8 (6.1%)	1 (2.1%)	0.232
Stress urinary incontinence*	3 (1.6%)	2 (1.5%)	1 (2.1%)	0.915

SG, standard prostate group; LG, large prostate group.
*All three patients had satisfactory results with a safety pad only within 3 months after surgery.

served between the SG and LG in efficacy variables, namely, total IPSS decrease (16.1 ± 8.7 vs. 14.8 ± 9.8, respectively; P = 0.408), voiding score decrease (7.8 ± 4.9 vs. 5.8 ± 5.7, respectively; P = 0.051), storage score de-

crease (5.1 ± 4.6 vs. 4.0 ± 5.3, respectively; P = 0.185), QOLS decrease (3.4 ± 1.6 vs 3.2 ± 1.8, respectively; P = 0.558), Qmax increase (10.9 ± 7.2 mL/s vs. 15.9 ± 14.1 mL/s, respectively; P = 0.182), and rate of PSA decrease (89.1% ± 11.2% vs. 89.9% ± 14.8%, respectively; P = 0.342).

The rate of early complications did not differ between the SG and LG groups (6.1% vs. 2.1%, respectively; P = 0.232). Postoperative serum sodium decrease in SG and LG was 5.1 ± 2.7 mEq/L and 2.7 ± 2.1 mEq/L, respectively (P = 0.295). Postoperative Hb decrease in SG and LG was 1.4 ± 0.2 g/dL and 1.0 ± 0.4 g/dL, respectively (P = 0.423). Regarding perioperative late events, urethral stenosis was more frequent in SG but did not differ significantly from that of LG (6.8% vs. 2.1%, respectively; P = 0.161) (**Table 2**).

Discussion

Since its introduction to clinical practice, TUEB has been widely adopted as an alternative to standard TURP, as it has equivalent efficacy and less comorbidity[9] and has generated significant interest and expectations among urologists worldwide, primarily because of its advantages of bipolar electrocautery and the superiority of enucleation over resection[10]. Studies have revealed its greater efficacy and safety as compared with other procedures for BPH in larger prostates[10–12]; however, only a few studies documented its efficacy for smaller prostates[13,14]. Therefore, we evaluated outcomes in relation to PV in patients with BPH who received TUEB and found that TUEB was an excellent surgical option for BPH treatment, regardless of prostate size.

In a previous study, TUEB improved IPSS by 14.5 points, QOLS by 3.8 points, and Qmax by 16.8 mL/s and reduced PSA by 82.6%[9]. Regarding safety, mean postoperative Hb level decreased by 1.08 ± 0.28 mg/dL and overall AE rate by 21.7%, with no patient requiring blood transfusion[15]. In our sample, IPSS significantly improved by 14.8 points, QOL by 3.3 points, Qmax by 11.3 mL/s, and PSA by 89.4%. Safety was also demonstrated by the 0.9 ± 0.15 mg/dL reduction in postoperative Hb level, an overall AE rate of 22% during the study, and the fact that no patient required blood transfusion. Therefore, the efficacy and safety in the cohort was comparable to that in previous reports.

Why is TUEB more effective and safer than regular TURP? In TUEB, the blood supply of the tissue is cut off when the tissue is enucleated and separated from the surgical capsule, while in TURP, blood vessels need to be repeatedly cut until the surgical capsule is reached. Therefore, blood loss is lower in TUEB than in TURP. In addition, this enucleation technique allows complete resection of the transitional zone, thus reducing the risk of recurrence as compared with TURP. Saline irrigation prevents water intoxication, a complication of TURP, which is one reason why TUEB is safe. In sum, TUEB is effective and results in fewer complications and a shorter recovery time[16].

Traditionally, prostatectomy (OP) with removal of enlarged hypertrophic tissue digitally has been the gold standard for large BPH and has yielded good long-term outcomes[17]. TUEB is an advanced form of this enucleation technique. It was reported to be an effective procedure for larger prostates, as was OP[18]. In contrast, only a few studies have documented its efficacy for smaller prostates[14]. Furthermore, few studies have compared the effects of prostate size on efficacy and safety. Therefore, we compared the efficacy and safety of TUEB between SG and LG and found that although total operative time was significantly longer for LG, no significant difference was observed between SG and LG in efficacy or safety variables. Recently, a similar result was reported[19]. When 172 patients undergoing TUEB were divided into three groups according to PV (<60 mL, 61-110 mL, and >110 mL), there was no significant difference between the three groups in efficacy variables (IPSS, ICIQ-SF, Qmax, PVR, and IIEF-EF) or safety variables (catheter insertion time, residence time hemoglobin decrease, and overall complication rate)[19].

As mentioned above, endoscopic enucleation is highly effective for treating BPH[20]; however, an unfavorable complication, transient SUI (tSUI), has been reported after TUEB and HoLEP in 1.4-44% of cases[21]. Almost all patients who developed SUI spontaneously recovered within 1 year, but it is one of the most common complaints affecting patient satisfaction and quality of life postoperatively[22]. Larger prostates often result in longer operations, leading to increased endoscopic manipulation and greater tSUI risk because of sphincter damage. In addition, complete tissue removal by enucleation leads to a larger prostate fossa. The larger the prostatic fossa, the more urine will accumulate, and the more urine will leak when abdominal pressure is applied[23]. A previous study reported that age, PV, and PSA reduction rate are risk factors for postoperative urinary incontinence in TUEB[24]. To reduce tSUI by decreasing endoscopic manipulation damage to the sphincter, EVP is becoming the choice over endoscopic enucleation[21]. However, the incidence of

tSUI reported by PVP, one of the common EVPs using potassium titanate phosphate laser, was 2.5%[25], while the incidence of tSUI by TUEB in this study, 1.6%, was comparable. Thus, we believe that the rate of tSUI after TUEB is acceptable.

Our study has several limitations, including its retrospective single-center design, small sample size, and short follow-up period. Further studies involving larger samples and longer follow-up are necessary to confirm our results. Furthermore, our study lacked data on comorbidities, urodynamics, and sexual function. Despite these limitations, this study provides new insights on the favorable efficacy and safety profile of TUEB for BPH treatment regardless of PV.

Conflict of Interest: None declared.

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