



Clinical Outcome of Endoscopic Enucleation of the Prostate Compared With Robotic-Assisted Simple Prostatectomy for Prostates Larger Than 80 cm³ in Aging Male

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Abstract

This study investigated and compared the surgical outcomes of using endoscopic enucleation (thulium: YAG laser and bipolar plasma; ThuLEP) with robotic-assisted simple prostatectomy (RASP) in the treatment of prostates larger than 80 cm³. Records were obtained for the period from January 2014 to December 2020 for selected patients with BPO who underwent RASP, ThuLEP, or bipolar transurethral enucleation of the prostate (B-TUEP). Patients were excluded if they had active malignant disease, neurogenic bladder, lower urinary tract syndrome for reasons other than BPO, and a history of prostate surgery. Data of 396 patients who underwent B-TUEP, ThuLEP, and RASP were examined. A total of 112 patients met the including criteria, 85 of whom (B-TUEP: 29; ThuLEP: 41; RASP: 15) completed the final visit. The mean operation time and duration of postoperative hospital stays in the RASP group were significantly longer than those of the B-TUEP and ThuLEP groups. Only 1 patient in the RASP group required blood transfusion. The RASP group was superior to the other groups in voiding improvement including Qmax and IPSS voiding score. The pain score of the ThuLEP group after surgery was significantly lower than that of the other two groups during hospitalization, whereas the QoL scores were identical between the three groups at 2 weeks, 3 months, and 6 months post operation. The rates of returning to ER within the first postoperative month did not differ significantly between the three groups, and all the reasons for return involved minor complications that required no additional invasive treatment. These three surgical methods (B-TUEP, ThuLEP, and RASP) are all effective and safe for treating prostates larger than 80 cm³, with each having its particular advantages. B-TUEP requires the shortest operation time, ThuLEP causes the lowest postoperative pain, and RASP results in superior voiding function improvement.

Keywords

prostate hypertrophy, laser, robotic surgery, outcome

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Introduction

Benign prostatic hyperplasia (BPH), which affects approximately 210 million men worldwide, is the main cause of lower urinary tract symptoms (LUTS) in the aging male population (Verhamme et al., 2002). Although alpha-1 blockers are used as first-line treatment of BPH

in men with LUTS (Davidian, 2016), patients with symptoms such as urinary retention, chronic urinary tract infections (UTIs), the involvement of bladder stones or diverticula, and renal insufficiency, as well as those who failed to respond to medication, are candidates for surgery (Oelke et al., 2013). Surgery for enlarged prostates is



challenging because postoperative bleeding and morbidity are related to the size of prostate glands (Uchida et al., 1999). Open simple prostatectomy (OSP) has long yielded the most favorable overall functional outcomes and durability among the various operative techniques for enlarged prostate surgery, but it is also associated with higher perioperative morbidity and costs (Tubaro & de Nunzio, 2006). Although no definite cutoff volume exists for large prostate glands, current European Association of Urology guidelines recommend OSP as the first-line treatment in men with bladder outlet obstruction (BPO) and a prostate larger than 80 cm³ (Rocco et al., 2011). However, the trend of surgical methods for enlarged prostates changed after Sotelo et al. published the first sequence of robotic-assisted simple prostatectomy (RASP) in 2008, demonstrating its effectiveness and benefits over the conventional open procedure (Sotelo et al., 2008). In later published research, RASP was demonstrated to be safe and efficient, with the advantages of minimal invasiveness and favorable short-term functional results compared with open methods (Kordan et al., 2020; Sotelo et al., 2008). By contrast, numerous studies have revealed that even in cases of larger prostates (>80 cm³), new endoscopic techniques (e.g., bipolar transurethral resection of the prostate, enucleation, and laser treatment) have similar safety and surgical outcomes as in cases of smaller prostates (Hueber et al., 2015; Joshi et al., 2014; Lotfi et al., 2020; Netsch et al., 2014). The goal of our study was to investigate and compare the surgical outcomes of endoscopic enucleation (thulium: YAG laser and bipolar plasma) to RASP in the treatment of enlarged prostates.

Material and Methods

Data Collection

Records for the period from January 2014 to December 2020 were obtained for selected patients with symptomatic BPH who underwent RASP, 120-W thulium: YAG laser (Vela XL) prostate enucleation (ThuLEP), or bipolar plasma enucleation of the prostate (B-TUEP) in the

geriatric urology department of (IRB number: 201800120B0, record from 2018 to 2020), Taiwan, following institutional review board approval. All procedures were performed by a single surgeon experienced in the aforementioned three procedures. Patients were free to select the method of treatment and provided signed consent forms. All patients underwent a thorough evaluation before surgery, including a medical history interview, physical examination, digital rectal examination (DRE), serum prostate-specific antigen (PSA) evaluation, and transrectal ultrasound (TRUS). If an abnormality was noted during the DRE or TRUS, the patient underwent a TRUS biopsy to rule out prostate cancer. Voiding volume (VV), postvoid residual urine volume (PVR), peak flow rate (Q_{max}), International Prostate Symptom Score (IPSS), and IPSS Quality of Life (QoL) score were also recorded to assess the voiding ability in patients. The inclusion criteria were as follows: Eastern Cooperative Oncology Group performance status ≤ 1 (Oken et al., 1982), age between 55 and 90 years, IPSS ≥ 20 , $Q_{max} \leq 15$ mL/s, and prostate volume ≥ 80 g. All patients met the surgical criteria for BPO (Oelke et al., 2013) and had been receiving medical treatment for at least 3 months prior to surgery. Patients were excluded if they had active malignant disease or a history of prostate surgery. Patients who developed neurogenic bladder or LUTS for reasons other than BPH were also excluded. This study was approved by Chang Gung Medical Foundation Institutional Review Board (IRB number: 201800120B0).

Surgical Equipment and Techniques

An Olympus SurgMaster UES-40 bipolar generator and OES-Pro bipolar resectoscope (Olympus Europe, Hamburg, Germany) were used for operations in the B-TUEP cohort. The standard energy settings for cutting and coagulation were 200 and 120 W, respectively. The enucleation and resection energies were 60 and 120 W, respectively. The surgical technique followed the procedure presented by Liu et al. (2010). All laser enucleation procedures were performed using a 120-W thulium laser (Vela XL, Boston Scientific, Marlborough, MA, USA)

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with a continuous wavelength of 1.94 μm . A LightTrail single-use laser fiber with a wavelength of 600 μm was employed. The fiber was introduced using an Olympus 26F continuous-flow resectoscope. Irrigation with a 0.9% sodium chloride solution was used in all processes. The enucleated prostate tissue was ground using a Wolf Piranha morcellator. The technique used in the ThuLEP group was described by Herrmann et al. (2010). All RASP procedures were performed using the da Vinci Si Surgical System (Intuitive Surgical Inc., Sunnyvale, CA, USA) and employed a suprapubic and transvesical method described by Leslie et al. (2014)

Postoperative Care

A three-way Foley catheter (22 Fr) was placed in the bladder at the end of all procedures to provide continuous irrigation. Catheter balloon traction to compress the prostate for hemostasis was not performed. Catheters were scheduled to be withdrawn on postoperative day 2 in the B-TUEP and ThuLEP groups and on postoperative day 7 in the RASP group, unless unexpected adverse events occurred that required delayed catheter removal. Antibiotics were used prophylactically and postoperatively in accordance with the guidelines (Dasgupta et al., 2009). When a patient demonstrated signs of postoperative infection, suitable antibiotics were provided on the basis of bacterial culture and drug sensitivity reports. The standard analgesic regimen was 7 days of acetaminophen for each group. On postoperative days 1 and 2, pain was assessed using the numeric rating scale (NRS). Regardless of the combination of urological medications used prior to surgery, 0.4 mg tamsulosin once daily was administered to all patients for 1 week. The physician determined whether to continue medication according to the patient's voiding status during the follow-up.

Evaluation and Follow-Up of Surgical Outcomes

The operating time, surgical complications, analgesic consumption, and NRS pain score (Hartrick et al., 2003) were documented as perioperative outcomes. Patients returned for follow-up visits at 2 weeks, 3 months, and 6 months postprocedure. The IPSS, QoL, Q_{max} , VV, and PVR scores were assessed during the visits and any complications were documented. Patients were asked to return to the clinic for treatment and intervention if they experienced any problems after 6 months of follow-up.

Statistical Analysis

All parameters are presented as means (standard deviation) and number (percentage). The chi-square test was

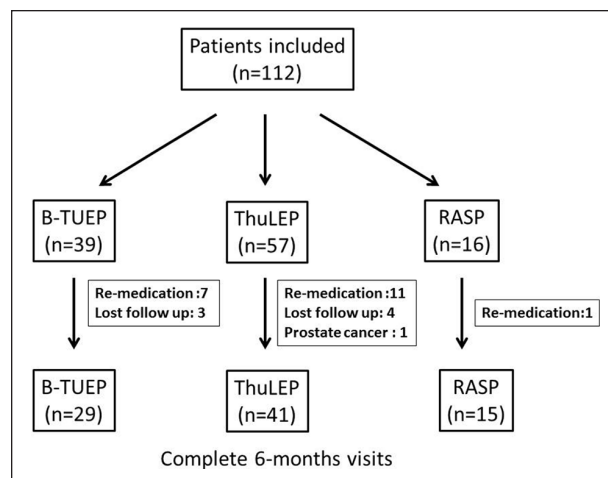


Figure 1. Flowchart of Patient Treatment.

used to analyze qualitative variables, and analysis of variance (ANOVA) was used for analyzing quantitative variables. Post hoc tests (Dunnnett's test) were used to clarify the differences among the three groups if the one-way ANOVA revealed statistically significant results. A repeated-measures ANOVA was employed to compare the means of the NRS scores. The significance level for all statistical analyses was $p < .05$. Data were analyzed using SPSS Statistics for Windows, version 25.0.

Results

Data from 396 patients who underwent B-TUEP, ThuLEP, and RASP were examined. A total of 112 patients met the inclusion criteria, and 85 of these patients (B-TUEP: $n = 29$, ThuLEP: $n = 41$, and RASP: $n = 15$) completed the final follow-up. The flowchart of patient treatment is illustrated in Figure 1. The baseline characteristics of the patients are summarized in Table 1. Patients who received RASP were younger ($p = .016$) and had larger prostates compared with the B-TUEP and ThuLEP groups ($p < .001$). The three groups were identical in the rate of urinary retention and distribution of medical comorbidities. The preoperative urinary conditions are described in Table 2. No statistically significant differences were observed in the initial total IPSS, IPSS QoL score, maximal urinary flow rate, or postvoid residual urine (RU) between the three groups. All patients received α blockers prior to surgery, with mean treatment durations of 19.5 (B-TUEP), 16.5 (ThuLEP), and 18.0 (RASP) months. The intraoperative and perioperative data are depicted in Table 3. The mean operation time of the RASP group was significantly longer than that of the B-TUEP and ThuLEP groups (192.5 vs. 99.2 vs. 119.1 min, $p < .001$). The duration of postoperative hospitalization in

Table 1. Baseline Patient Characteristics.

Parameter (M, SD)	B-TUEP (n = 29)	ThuLEP (n = 41)	RASP (n = 15)	p value	Post hoc
Age (years)	73.45 (6.82)	71.88 (8.51)	66.40 (6.42)	.016	B-TUEP > RASP ThuLEP > RASP
PSA ($\mu\text{g/L}$)	11.99 (8.58)	8.70 (7.47)	10.44 (5.38)	.214	
Prostate volume (mL)	94.26 (14.75)	89.83 (7.80)	116.37 (17.99)	<.001	RASP > B-TUEP RASP > ThuLEP
Prostate T zone (mL)	48.89 (15.42)	41.41 (12.18)	72.22 (15.89)	<.001	RASP > B-TUEP > ThuLEP
Medication duration (months)	19.4 (36.8)	16.5 (24.5)	18.1 (15.7)	.913	
Urinary retention (n, %)	10 (34.5)	17 (41.5)	4 (26.7)	.573	
Comorbidities (n, %)					
DM	7 (24.1)	10 (24.4)	2 (13.3)	.652	
HTN	17 (58.6)	22 (53.7)	4 (26.7)	.114	
CAD	6 (20.7)	2 (4.9)	0 (0.0)	.046	
Arrhythmia	3 (10.3)	5 (12.3)	0 (0.0)	.536	
Stroke	5 (17.2)	6 (14.6)	0 (0.0)	.295	
CRI	4 (13.8)	3 (7.3)	0 (0.0)	.277	

Note. B-TUEP = bipolar transurethral enucleation of the prostate; ThuLEP = thulium laser enucleation of the prostate; RASP = robotic-assisted laparoscopic simple prostatectomy; SD = standard deviation; PSA = prostate-specific antigen; DM = diabetes mellitus; HTN = hypertension; CAD = coronary arterial disease; CRI = chronic renal insufficiency.

Table 2. Preoperative Urinary Condition of the Patients.

Parameter (M, SD)	B-TUEP (n = 29)	ThuLEP (n = 41)	RASP (n = 15)	p value	Post hoc
IPSS (total)	25.31 (4.77)	25.05 (5.46)	26.27 (5.12)	.738	
IPSS (voiding)	14.62 (2.92)	16.15 (3.05)	17.20 (3.95)	.029	RASP > B-TUEP
IPSS (storage)	10.69 (3.07)	8.90 (3.38)	9.07 (1.75)	.049	
IPSS (QoL)	5.00 (0.71)	5.10 (0.66)	5.33 (0.62)	.299	
Qmax (mL/s)	7.11 (3.74)	6.68 (4.12)	5.40 (1.80)	.344	
VV (mL)	155.89 (90.11)	182.73 (94.31)	115.07 (50.62)	.041	ThuLEP > RASP
PVR (mL)	127.14 (126.98)	155.27 (152.65)	185.80 (131.58)	.418	
Medication (n, %)					
α -blockers	29 (100)	41 (100)	15 (100)		
5-ARI	6 (20.7)	5 (12.2)	4 (26.7)	.394	
Anti-muscarinics	7 (24.1)	4 (9.8)	2 (13.3)	.267	
beta 3 agonist	1 (3.4)	1 (2.4)	0 (0.0)	1.000	
Bethanecol	3 (10.3)	7 (17.1)	3 (20.0)	.673	

Note. B-TUEP = bipolar transurethral enucleation of the prostate; ThuLEP = thulium laser enucleation of the prostate; RASP = robotic-assisted laparoscopic simple prostatectomy; IPSS = international prostate symptom score; QoL = quality of life; Q_{max} = maximum flow rate; VV = voiding volume; PVR = postvoiding residual urine volume; 5-ARI = 5 alpha reductase inhibitors.

the RASP group was also significantly longer than in the B-TUEP and ThuLEP groups (3.9 vs. 2.5 vs. 2.2 days, $p < .001$). RASP removed a higher percentage of prostatic tissue compared with the other two techniques (84% vs. 61% [B-TUEP] vs. 69% [ThuLEP], $p = .16$). No patients in the B-TUEP or ThuLEP groups received blood transfusions during the entire treatment course, whereas 1 patient in the RASP group required blood transfusion. Only 1 patient (6.7%) in the RASP group presented with UTI, and the UTI rate was significantly

lower in the RASP group than in the B-TUEP (48.3%) and ThuLEP (58.7%) groups ($p = .006$). The rates of emergency room return visits within 1 month after operation were 13.8% in the B-TUEP group, 14.6% in the ThuLEP group, and 6.7% in the RASP group, with no statistically significant differences between groups. The rates of recatheterization and prolonged analgesics use between the three cohorts were also not significantly different. No patients complained of prolonged stress or urge incontinence in our study cohorts.

Table 3. Intraoperative and Perioperative Data.

Parameter	B-TUEP (n = 29)	ThuLEP (n = 41)	RASP (n = 15)	p value	Post hoc
OP time (min)	99.24 (27.89)	119.07 (27.15)	192.53 (27.78)	<.001	RASP > ThuLEP >B-TUEP
Hospitalization duration (days)	2.48 (0.78)	2.20 (0.46)	3.93 (1.58)	<.001	RASP > B-TUEP RASP > ThuLEP
Percentage of tissue removed (%)	61% (0.24)	69% (0.29)	84% (0.10)	.016	RASP > B-TUEP RASP > ThuLEP
Transfusion (n, %)	0 (0.0)	0 (0.0)	1 (6.7)	.176	
Re-catheterization <1 month (n, %)	1 (3.4)	7 (17.1)	1 (6.7)	.181	
Additional narcotic use (n, %)	7 (24.1)	4 (9.8)	0 (0.0)	.072	
Analgesic requirement >1 week (n, %)	5 (17.2)	7 (17.1)	1 (6.7)	.728	
UTI < 1 month (n, %)	14 (48.3)	22 (53.7)	1 (6.7)	.006	B-TUEP > RASP ThuLEP > RASP
Returned to ER < 1 month (n, %)	4 (13.8%) Hematuria: 2 UTI:1 Herpes Zoster: 1	6 (14.6%) UR: 2 UTI: 3 Dizziness: 1	1 (6.7%) UR:1	.832	

Note. B-TUEP = bipolar transurethral enucleation of the prostate; ThuLEP = thulium laser enucleation of the prostate; RASP = robotic-assisted laparoscopic simple prostatectomy; OP = operation; UR = urinary retention; UTI = urinary tract infection.

The changes in urodynamic parameters are displayed in Figure 2. Among the three groups, Q_{max} , VV, and PVR demonstrated significant improvement. The level of Q_{max} improvement observed in the third and sixth months after operation in the RASP group patients was significantly higher than that of the other two groups (Figure 2A). The VV improvement of the RASP group was significantly greater than that of the other two groups at the 3-month postoperative evaluation (Figure 2B). No significant differences were observed in the amount of change in PVR between the three groups (Figure 2C). The changes in IPSS values are presented in Figure 3. Although the change in total IPSS at the three visit time points did not differ significantly between groups (Figure 3A), the change in the IPSS voiding score of the B-TUEP group at 2 weeks and 3 months postoperation was significantly lower than that of the ThuLEP and RASP groups (Figure 3B). In addition, no significant differences were noted among the three groups in the change in IPSS storage scores at the three observation time points (Figure 3C). The changes in QoL scores at the three visit time points did not differ significantly between the three groups (Figure 4).

The mean NRS pain scores on postoperative day 1 were 1.38 in the B-TUEP group, 0.37 in the ThuLEP group, and 2.13 in the RASP group ($p < .001$, post hoc test: ThuLEP < B-TUEP and ThuLEP < RASP; Figure 5). The mean NRS pain scores on postoperative day 2 were 0.93 in the B-TUEP group, 0.17 in the ThuLEP group, and 1.40 in the RASP group ($p < .001$, post hoc

test: ThuLEP < B-TUEP and ThuLEP < RASP). The aforementioned data indicate that the pain scores of the ThuLEP group after surgery were significantly lower than those of the other two groups. The postoperative PSA levels in all three groups decreased markedly, but no significant differences were observed in this reduction between groups. The mean PSA declines at 3 months postoperation in the B-TUEP, ThuLEP, and RASP groups were 10.5, 5.5, and 8.7 ng/mL, respectively ($p = .575$), and the mean PSA declines at 6 months postoperation in the B-TUEP, ThuLEP, and RASP groups were 11.5, 5.8, and 9.4 ng/mL, respectively ($p = .533$).

Discussion

Despite the observation that OSP appears to be a safe treatment for enlarged prostates ($>80 \text{ cm}^3$), this technique is frequently associated with high rates of perioperative transfusion and complications, including myocardial infarction, bladder neck obstruction, wound infection, and clot retention (Ahmed Gadani, 2012; Ngugi et al., 2007; Suer et al., 2008; Zargooshi, 2007). Thus, over the last few decades, numerous innovative technologies have been developed as substitutes for the classic OSP in an attempt to achieve safer and more effective treatment outcomes. According to a recent study by Banapour et al. (2014), RASP provided similar clinical outcomes to OSP but with a shorter hospital stay and lower risk of perioperative bleeding, blood transfusion, and postoperative complications. Furthermore, current guidelines list

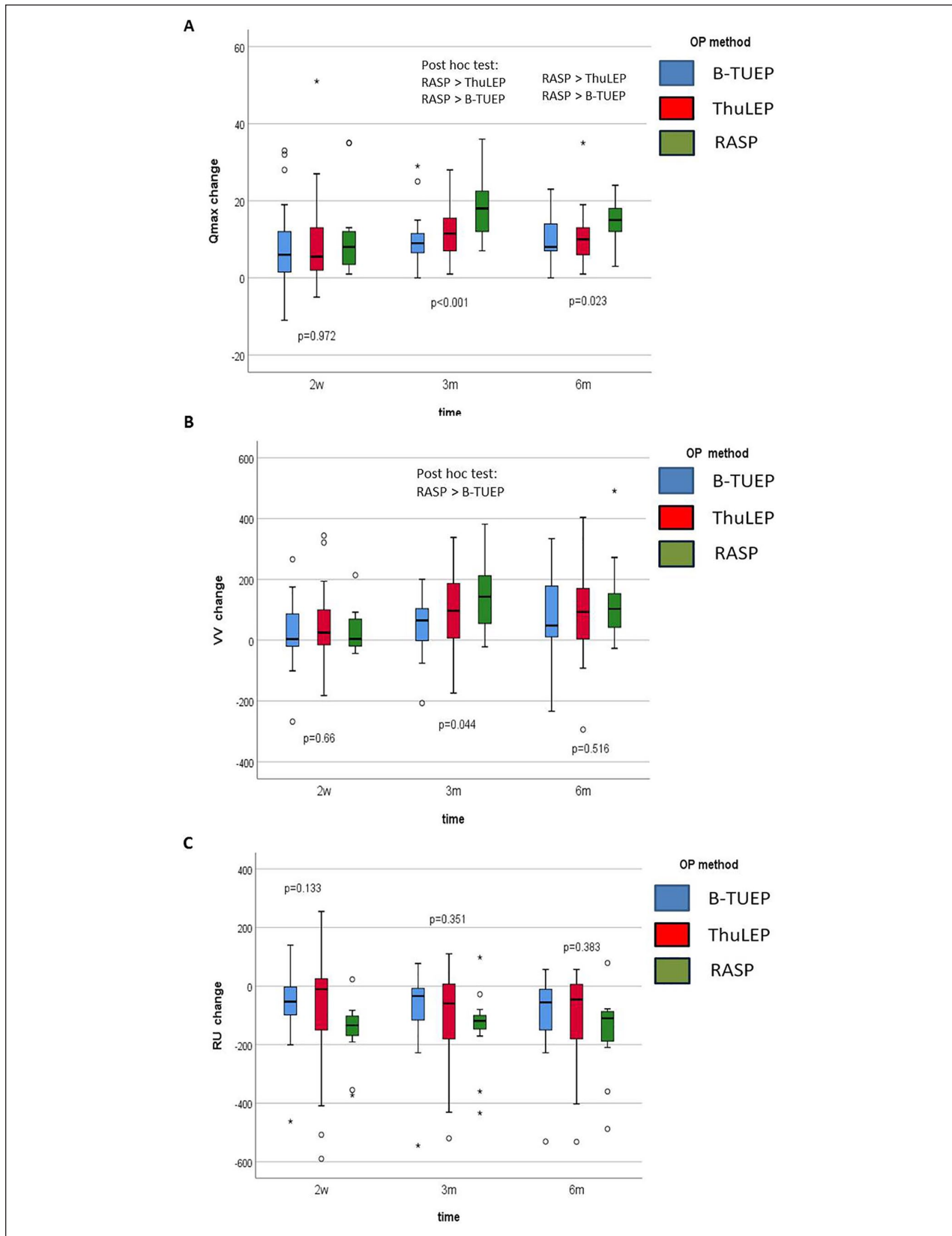


Figure 2. (A) Change in Maximal Flow Rate (Q_{max}) of the Three Groups; (B) Change in Voiding Volume (VV) of the Three Groups; (C) Change in Postvoiding Residual Urine (RU) of the Three Groups.

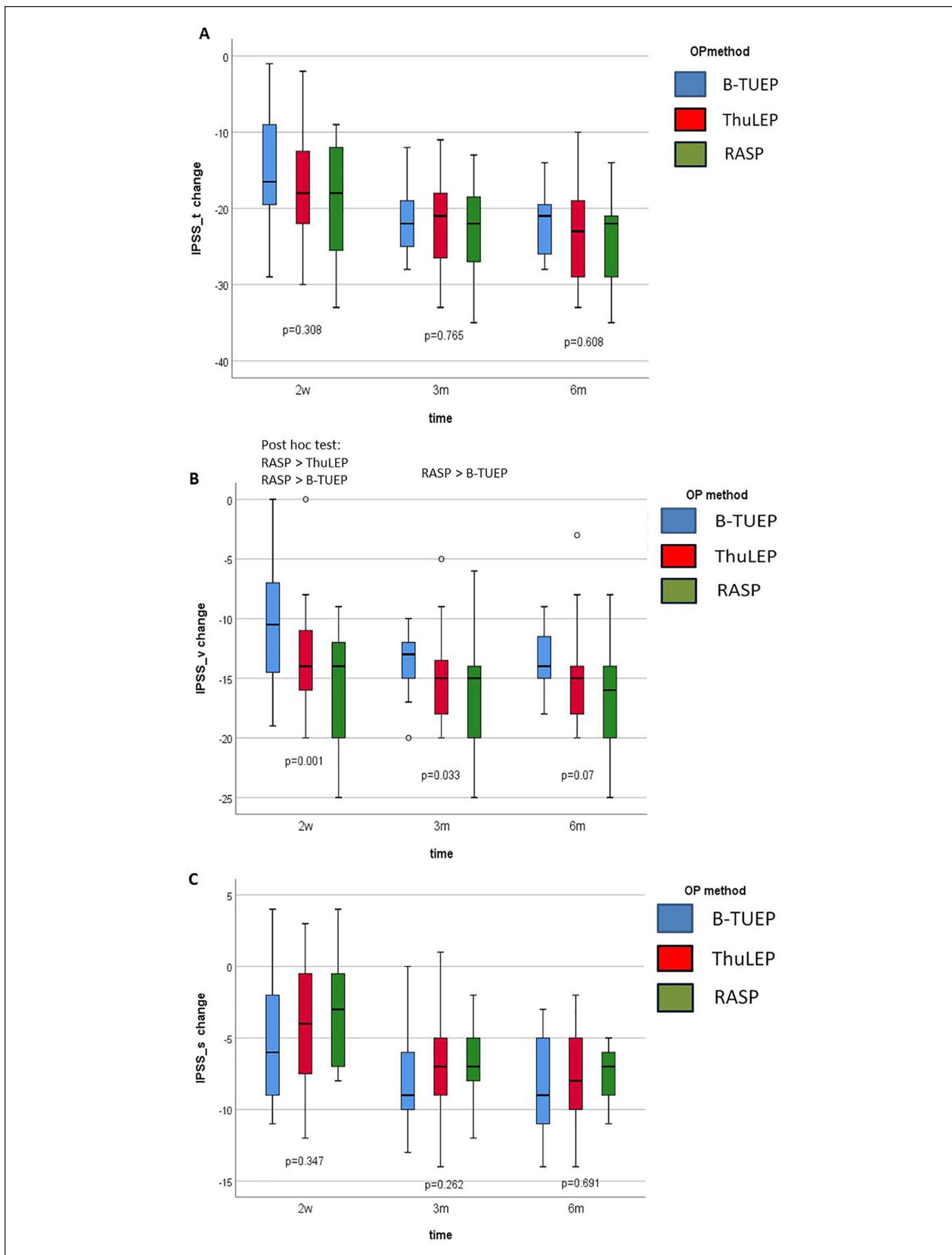


Figure 3. (A) Change in Total IPSS; (B) Change in IPSS Voiding Score; (C) Change in IPSS Storage Score.

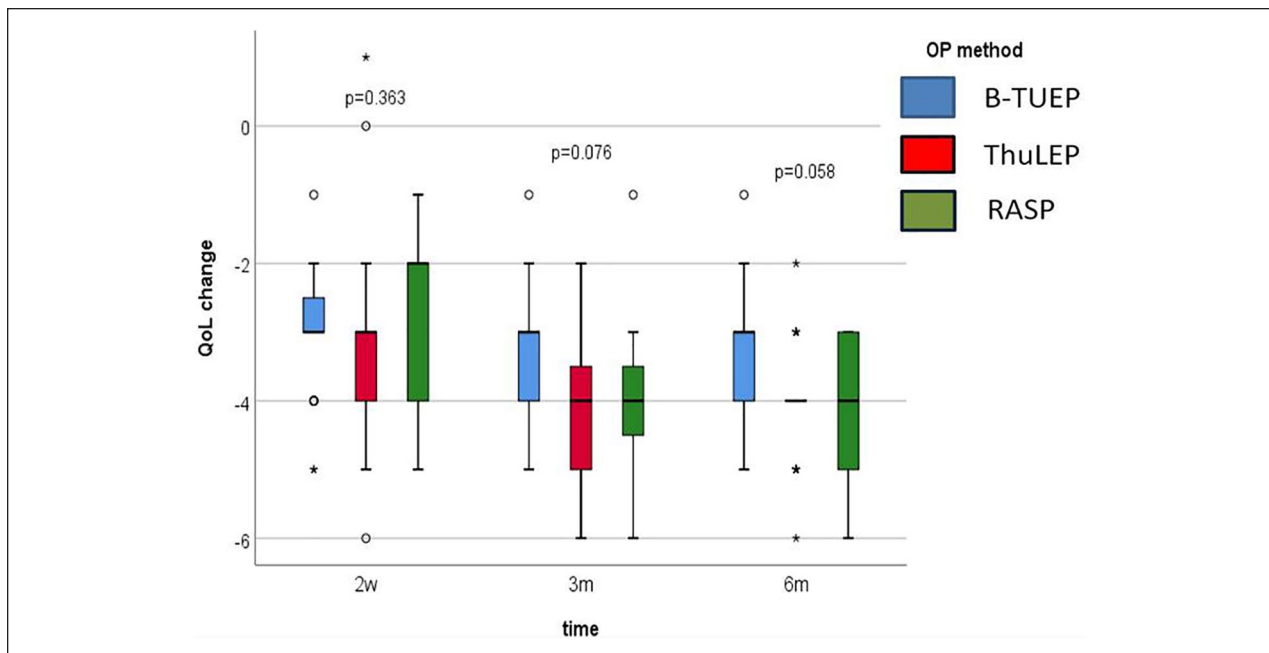


Figure 4. Change in Quality of Life (QoL) Scores.

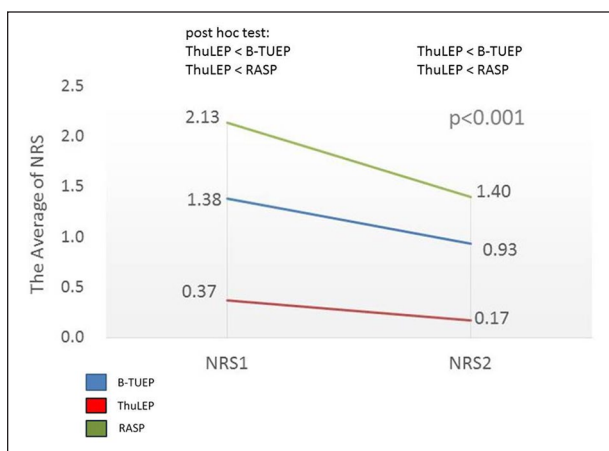


Figure 5. Numeric Rating Scale on Postoperative Days 1 and 2.

conventional laparoscopic and robotic-assisted simple prostatectomy as investigational procedures, with a level 3 degree of evidence and a recommendation grade of C (Patel et al., 2014). Despite the uncertainty regarding its effectiveness and safety, transurethral endoscopic surgery may be selected instead of simple prostatectomy to treat prostate hypertrophy larger than 80 cm³ in daily practice because it is convenient and less invasive. To the best of our knowledge, only one related study compared transurethral endoscopic surgery to robotic surgery in BPO treatment for prostates larger than 80 cm³.²⁶ In that study, comparison of RASP with holmium laser enucleation of the prostate revealed similar surgical outcomes, but the catheterization duration and median hospitalization were

slightly shorter in the holmium laser group (Umari et al., 2017). Therefore, the goal of our study was to investigate and compare the surgical outcomes of endoscopic enucleation (thulium: YAG laser and bipolar plasma) to RASP in the treatment of extra-large prostates.

Each of the patients in our study met the surgical criteria for BPO, and the mean medical treatment duration before surgery was more than 1 year (B-TUEP 19.4 months, ThuLEP: 16.5 months, and RASP: 18.1 months), indicating that the patients had severe symptoms that were not relieved by medical treatment. In addition to patients who were lost to follow-up during the study, we also excluded patients whose pathology reports indicated prostate cancer and those who continued taking urological medication because of clinical needs, as these treatments would interfere with our follow-up evaluation. We found that the three surgical methods were safe and effective, but the operation time and postoperative hospital stay of the RASP group were significantly longer than those of the other two groups. Only one patient in the RASP group, and none in the other two groups, required blood transfusion during hospitalization. Moreover, we found that RASP removed a greater proportion of prostate adenoma than the other two procedures, resulting in a greater improvement in Q_{max} and IPSS voiding score. Our findings support the results of L. K. Huang et al. (2019), who indicated that more radical resection resulted in more improved voiding functions.

The major difference between our study and related studies is that we assessed the patients' postoperative pain scores, analgesics usage, and changes in QoL scores.

When using the same postoperative analgesics, the three groups of patients had the same rates of prolonged oral analgesic requirements and additional intravenous or intramuscular narcotic use. However, the pain index on postoperative days 1 and 2 differed significantly between the three groups. The patients in the ThuLEP group indicated significantly lower pain scores than did those in the other two groups. A recent study revealed that enucleation of the prostate using the 120-W thulium laser yielded lower postoperative pain and greater improvement in short-term QoL after surgery compared with bipolar resection of the prostate (Hou et al., 2020). Our research found that this phenomenon also occurred for operations on prostates larger than 80 cm³. The 120-W thulium laser also yielded lower postoperative pain scores than RASP. We believe that the difference in pain scores was primarily due to the depth of thermal penetration. According to the literature, the average depth of thermal damage to prostate tissue induced by plasma kinetics is 2.4 ± 0.84 mm (range: 0.3–3.5 mm), whereas the absorbed energy of the thulium laser at the tissue surface causes instant vaporization and limits the penetration depth to less than 0.2 mm (X. Huang et al., 2008; Maddox et al., 2012).

Because of our specific research approach, our study has several limitations. First, this was not a randomized study, and our patients were free to select their treatment methods. Although no differences were observed in comorbidity between the three groups before surgery, we found that patients who opted for RASP were younger, possessed larger prostates, and had slightly different preoperative IPSS and urodynamic parameters. Therefore, to objectively analyze the therapeutic effects and reduce bias, we compared the change values of each parameter rather than the absolute value during the observation period. Second, our patients were not subjected to a pressure-flow urodynamic assessment (Gommer et al., 1999), which is regarded as the gold standard for identifying bladder outflow obstruction and provides additional information on voiding function. A randomized prospective study with a larger patient sample size is warranted to reinforce our research conclusions. Despite the aforementioned limitations, we consider our study to be valid and innovative because it is the first case-control study to compare three commonly used surgical techniques to treat extra-large prostates in terms of their efficacy, safety, postoperative pain, and improvement in QoL.

Conclusion

Our research found that these three surgical methods (B-TUEP, ThuLEP, and RASP) were effective and safe for enlarged prostates greater than 80 cm³, and each technique had specific advantages. Specifically, patients who received B-TUEP required the shortest operation time;

patients undergoing ThuLEP experienced less pain on postoperative days 1 and 2; and patients receiving RASP exhibited the greatest improvement in voiding function, especially in Q_{max} and IPSS voiding score, as well as the lower relative probability of UTI after surgery. Further randomized studies involving a larger number of patients are warranted to verify our findings.

Declaration of Conflicting Interests

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