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Application of En Bloc and Urethral Mucosal Flap Sparing Techniques Improve the Functional Outcomes in Holmium Laser Enucleation of Prostate: A Retrospective Case Control Study

Jizhi Zhou[1], Zengrong Hua[1], Min Tang[2], Xiaoxin Meng[2], and Pu Li[2]

Abstract

The purpose of the study was to study the feasibility of holmium laser enucleation of prostate (HoLEP) with en bloc and urethral mucosal flap sparing technique in treating benign prostatic hyperplasia (BPH) patients and to evaluate the influence of this modified technique on urinary function. A cohort of 188 BPH patients underwent HoLEP from June 2017 to October 2019. Among them, 92 patients underwent conventional en bloc HoLEP and the other 96 patients underwent HoLEP with en bloc and urethral mucosal flap sparing techniques. The basic characteristics, the volume of the prostate, urodynamic data, and perioperative parameters were recorded for comparison. The outcome parameters include international prostate symptom score (IPSS), maximum urinary flow rate (Qmax), post-voiding residual (PVR), quality of life score (QoL), and incidence of de novo stress urinary incontinence (SUI). The basic characteristics were equivalent in both groups. All HoLEP procedures were smoothly carried out. The perioperative complications were low and did not show a significant difference. The follow-up period was 12 months or longer. IPSS, Qmax, QoL, and PVR were improved postoperation in both groups. There was no statistical difference in the parameters between the two groups. When considering a postoperative SUI, the occurrence of short-term and long-term SUI in the modified HoLEP group was significantly less than those in the conventional HoLEP group ($p < 0.05$). In summary, HoLEP by using en bloc and urethral mucosal flap sparing technique is a safe and effective treatment for BPH patients, especially in preventing postoperative SUI.

Keywords

holmium laser enucleation of prostate, urethral mucosal flap sparing, benign prostate hyperplasia, stress urinary incontinence

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Introduction

Benign prostate hyperplasia (BPH) and associated lower urinary tract symptoms (LUTS) are common health problems in elderly males worldwide. The incidence of histologic BPH reaches to 50% in males in their 60s, and the rate rises to 90% in their 80s (Gratzke et al., 2015). Serious BPH/LUTS will incur significant morbidities and compromise the QoL in males if untreated (Launer et al., 2021).

Transurethral resection of prostate (TURP) was considered as the gold standard for surgical treatment of BPH in the past decades, but its shortcomings are prominent, such as significant bleeding, high recurrence rate, and transurethral resection syndrome (TURS). As the first described anatomic endoscopic enucleation of prostate (AEEP; Pirola et al., 2018), holmium laser enucleation of

[1]Department of Urology, Huaian Hospital of Huaian City, Huaian, China
[2]Department of Urology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China

Corresponding Author:
Pu Li, Department of Urology, The First Affiliated Hospital of Nanjing Medical University, 300 Guangzhou Road, Nanjing 210029, China.
Email: Lee_lipu@163.com

prostate (HoLEP) has received much attention and developed into true anatomical enucleation for prostate of any volume (Das et al., 2020; de Figueiredo et al., 2020; Oh & Shitara, 2020). It is because of the advantage over traditional therapies, HoLEP is widely adopted by patients seeking surgical treatment for BPH/LUTS (Xiao et al., 2019). Although HoLEP has a compatible functional outcome, the risk of postoperative de novo stress urinary incontinence (SUI) is often an issue of concern. Some researchers have proposed that de novo SUI after HoLEP may be caused by excessive damage to the external sphincter and bladder neck (Nam et al., 2015). Various modified techniques have been adopted to reduce the incidence of postoperative SUI, such as the "three horseshoe-like incisions" approach (Miernik & Schoeb, 2019). However, the role of these modifications in the prevention of postoperative SUI is unclear. In this present study, we performed HoLEP with two different techniques and evaluated the feasibility of the urethral mucosal flap sparing technique and associated surgical outcomes.

Materials and Methods

Patients

A total of 188 HoLEP cases in our department from June 2017 to October 2019 were included in this retrospective research. Patients were divided into two groups: 92 patients (conventional HoLEP group) underwent HoLEP with the conventional en bloc technique from June 2017 to August 2018, and 96 patients (HoLEP with mucosal sparing technique group) underwent HoLEP with the en bloc and urethral mucosal flap sparing technique from August 2018 to October 2019. All of the patients exhibited moderate (international prostate symptom score [IPSS] 8–19) to severe (IPSS>20) LUTS due to BPH. Patients with contraindications to surgery were excluded.

Clinical and Laboratory Assessment

The indicators of HoLEP were male patients with moderate to severe LUTS due to BPH with determinate prostatic enlargement. The QoL score and IPSS were acquired through questionnaire investigation by experienced residents. A baseline prostate-specific antigen (PSA) level was detected before the surgery. Patients with PSA $\geq$ 4 ng/L were checked by multiparameter magnetic resonance imaging (MRI) and biopsy. Patients with prostate cancer were excluded. Transrectal ultrasonography or MRI was used to detect prostatic volume. Post-void residual (PVR) was detected by ultrasonography. The pressure-flow study was performed before the surgery to determine the existing bladder outlet obstruction (BOO). Maximal flow rate (Qmax) and detrusor pressure at maximal flow (PdetQmax) were recorded. Bladder contractility index (BCI) and bladder outlet obstruction index (BOOI) were calculated by the following formula: BCI = PdetQmax + 5(Qmax), BOOI = PdetQmax − 2(Qmax) (Chen et al., 2019). Patients with obvious detrusor underactivity (BCI < 100) were excluded.

Surgical Procedures

All HoLEP procedures were performed by a surgeon (P.L.). The surgeon had more than 800 surgical cases before this study was carried out.

The procedure for HoLEP is applied with en bloc and urethral mucosal flap sparing techniques: The enucleation procedure was performed using an 80-W Ho: YAG laser set (Lumenis Inc., Yokneam, Israel) at 2.0 Joule with a frequency of 40 Hz, which was described previously (Li et al., 2021). Briefly, a 26-Fr resectoscope (Karl Storz, Tuttlingen, Germany) with a 550-μm end-fire optic fiber (Lumenis Inc, Yokneam, Israel) was inserted into the urethra and bladder under direct vision. An initial incision was made on either side around the proximal level of the verumontanum, in an inverted U-shape. Then, a glossy plane was exposed and expanded between the surgical capsule and hyperplastic gland. The middle lobe was partially elevated and the bilateral lobes were mechanically mobilized apically until it reached 11 o'clock at the right lobe and 1 o'clock at the left lobe. After this step, the mucosal strip between the external sphincter and hyperplastic gland was cut off, except for the mucosal strip at 12 o'clock. This mucosal strip was cut off at 1 cm from the inner side of the external sphincter to preserve this part of the mucosal flap. Subsequently, using the laser pulse and shaft of the resectoscope, the plane was carried bilaterally and forward between the hyperplastic gland and surgical capsule until the plane centrally converged at the anterior commissure. Continued to expand the plane toward the bladder neck and breakthrough into the bladder at 12 o'clock to create a "channel" between the anterior commissure and surgical capsule. Then, the incision of the bladder neck was carried to both sides along the arc. Some circular fiber could be revealed at about 0.5 cm nearby the bladder neck, which was shiny and white and visually different from the normal hyperplastic gland. This circular fiber was part of the internal sphincter that should be preserved. After the resection, the whole hyperplastic gland was dissociated and dropped into the bladder (Figure 1). Enucleated tissues were morcellated and exhausted with a tissue morcellator (Lumenis Inc., Yokneam, Israel).

The conventional HoLEP was analogous to that of the urethral mucosal flap sparing technique (Tang et al., 2020), except for treatment of the mucosal strip at 12

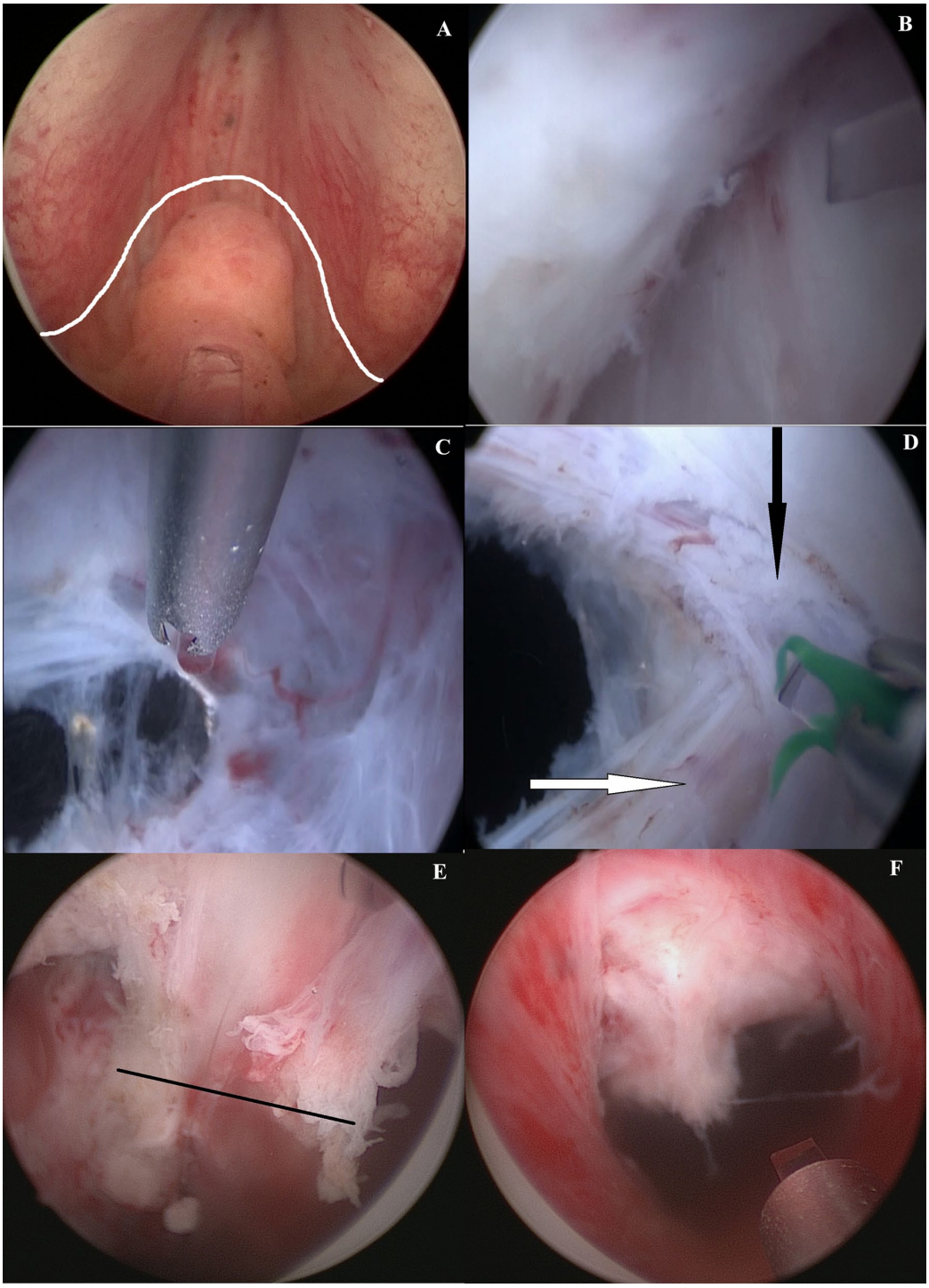

Figure 1. HoLEP Procedure Used an En Bloc and Urethral Mucosal Flap Sparing Technique: (A) An Initial Incision Was Made on Either Side Around the Proximal Level of the Verumontanum, in an Inverted U-Shape. (B) An Anatomic Layer Was Exposed and Expanded Between the Surgical Capsule and the Hyperplastic Gland. Right: Surgical Capsule; Left: Hyperplastic Gland. (C) The Hyperplastic Gland at the Anterior Commissure Was Stripped From the Bladder Neck to Break Through Into the Bladder at 12 O'clock. (D) The Tissue Is Visually Different When Approaching the Bladder Neck. The Gland That Needs to be Removed Was Actinomorphic (White Arrow), and the Bladder Neck Was Ring-Shaped (Black Arrow) Which Should Be Preserved. (E) Image of the Mucosa at the Sphincter. The Black Line Marked the Location of Dissection (1 cm Urethral Mucosal Flap Was Reserved). (F) Image of the Reserved Mucosal Flap After the Hyperplastic Gland Was Pushed Into the Bladder Cavity

Table 1. Comparison of the Baseline Parameters Between Observation Group and Control Group.

Factors	Observation group	Control group	*p* value
Number of cases (*n*)	96	92	
Preoperative			
Age	70.2 ± 9.5	69.4 ± 6.3	.49
Prostate volume (mL)	62.4 ± 23.5	62.9 ± 24.9	.89
Preoperative PSA (ng/mL)	3.1 ± 3.8	2.9 ± 2.4	.67
Diabetes disorder (*n*, %)	16(16.7)	12(13.0)	.54
BMI	24.2 ± 5.4	24.7 ± 6.2	.70
Preoperative catheterization (*n*, %)	7(7.3)	7 (7.6)	.93
IPSS	22.5 ± 4.6	23.4 ± 5.1	.21
QoL	5.0 ± 1.0	4.0 ± 1.0	.18
PVR (mL)	54.8 ± 69.9	62.4 ± 59.8	.42
Qmax (mL/s)	5.8 ± 2.5	5.4 ± 2.7	.29
BOOI	61.2 ± 32.4	62.6 ± 34.7	.77
BCI	96.4 ± 35.1	100.5 ± 46.3	.49

Note. Mean ± *SD* or no. pts. PSA = prostate specific antigen; BMI = body mass index; IPSS = international prostatic symptomatic score; QoL = quality of life; PVR = post-void residual volume; Qmax = maximum urinary flow rate; BOOI = bladder outlet obstruction index; BCI = bladder contractility index.

o'clock. This tissue was cut off close to the inner side of the external sphincter, to completely mobilize the prostatic apex.

Postoperative Treatment and Follow-Up

Detection of hemoglobin levels was performed 2-hr of postoperation and continuous bladder irrigation was kept until the first morning of postoperation. The Foley catheter was removed on the second day of postoperation. Patients were asked to accept follow-up procedures at 1, 6, and 12 months postoperation to determine IPSS, PVR, Qmax, and QoL. A 24-hr pad count (pads/day, PPD) was used in evaluating the severity of urinary incontinence (UI). Patients who did not complete 12-month follow-up were excluded from this study. The UI was defined as more than 2 PPD (Mühlstädt et al., 2017). The continence outcome was evaluated through a questionnaire during the follow-up visit. The type of UI was specified as being SUI, urge urinary incontinence (UUI), or mixed according to the symptoms. De novo SUI was defined as if one responded positively to stress-related issues rather than urge-related ones.

Statistical Analyses

Statistical analyses were performed with the SPSS software version 22 (IBM, NY, USA). Data were analyzed using Student's, Fisher's exact, chi-square, or Mann–Whitney *U* test according to the distribution. Quantitative data were expressed as mean ± standard deviation (*SD*). The $p < .05$ was considered statistically significant.

Results

The procedures of HoLEP were completed in all 188 cases without conversion to another surgical approach. The basic clinical characteristics were listed in Table 1. There were no statistical differences in the demographic details, including age ($p = .49$), prostate volume ($p = .89$), preoperative PSA level ($p = .67$), diabetes mellitus ($p = .54$), body mass index (BMI) ($p = .70$), preoperative catheterization rate ($p = .93$), IPSS ($p = .21$), and QoL ($p = .18$). Preoperative urodynamic parameters, including Qmax ($p = .29$), BOOI ($p = .77$), BCI ($p = .49$), and PVR ($p = .42$), were also similar in both groups (Table 1).

The perioperative parameters and complications were listed in Table 2. The average operative duration was similar between the two groups ($p = .45$). The mean losses of hemoglobin was 0.91 and 0.82 g/dL in HoLEP with mucosal sparing technique and conventional HoLEP groups, respectively, and there was no significant difference ($p = .15$). The average hospital stay was similar in the two groups ($p = .21$). The success proportion of the first attempt in removing the urinary catheters was also similar in the two groups ($p = .63$).

During the hospital stay, no major life-threatening complications were observed. No TURS was observed during and postoperation. No blood transfusion was conducted in both groups. Other long-term complications, including bladder neck contracture and urethral stricture, were infrequent and similar in the two groups ($p = .68$; Table 2).

During the follow-up, the postoperative IPSS and QoL decreased to a lower level and maintained stability (Figure

Table 2. Comparison of Perioperative Parameters and Complications Between Observation Group and Control Group.

Factors	Observation group	Control group	*p* value
Perioperative			
Operative duration (min)	89.3 ± 15.8	91.1 ± 16.7	.45
Change of hemoglobin at the first postoperative day (g/dL)	−0.91 ± 0.65	−0.82 ± 0.45	.15
Hospital stay (days)	5.0 ± 1.2	5.5 ± 1.4	.21
Success on the first void (*n*,%)	80 (83.3)	79 (85.9)	.63
Complications (*n*, %)			
TURS (*n*)	0	0	/
Blood transfusion (*n*)	0	0	/
Urethral stricture/bladder neck contracture(*n*, %)	3(3.1)	2(2.2)	0.68

Mean ± *SD* or no. pts (%). TURS = transurethral resection syndrome.

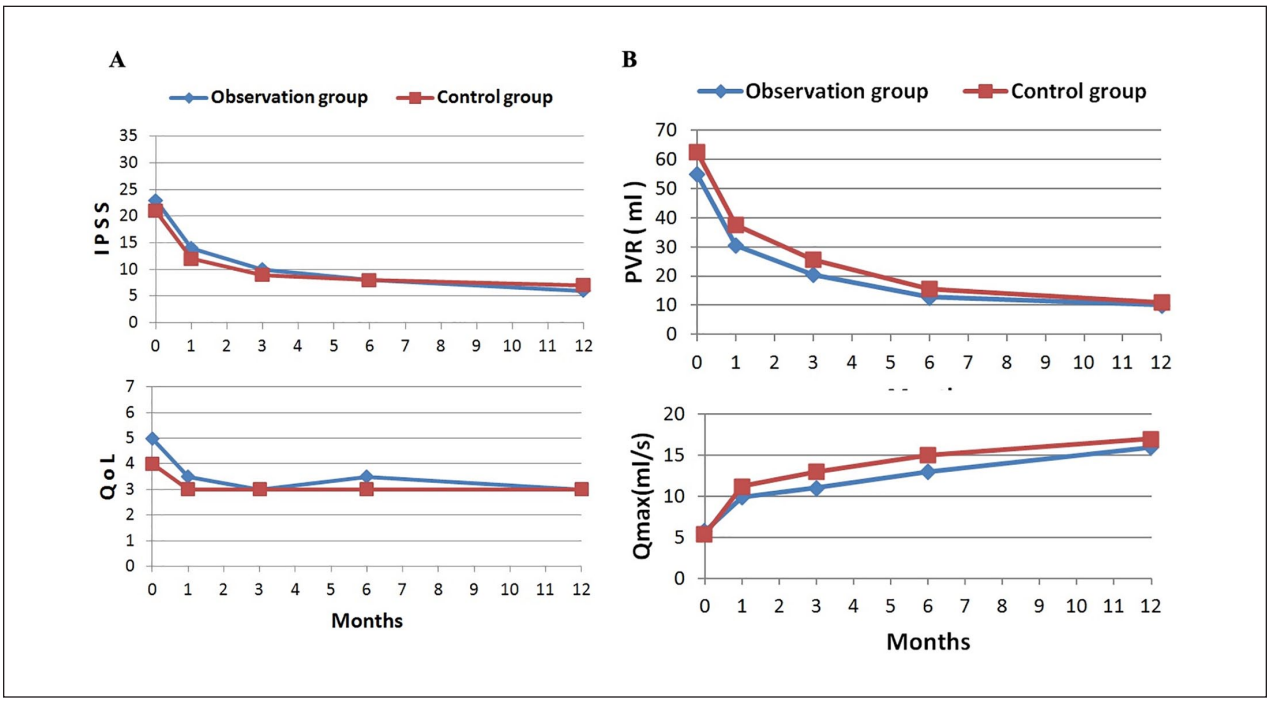

Figure 2. (A) Postoperative Variation of IPSS and QoL During Follow-Up. There Was No Statistical Difference Between the HoLEP With Mucosal Sparing Technique Group and the Conventional HoLEP Group (p > .05). The Improvements in IPSS and QoL Were Immediate and Lasting During the Follow-Up Session. (B) Postoperative Variations of PVR and Qmax During Follow-Up. There Were No Statistical Differences Between HoLEP With Mucosal Sparing Technique Group and the Conventional HoLEP Group (p > .05). Both Groups Exhibited Significant Improvement in PVR and Qmax in the First Month and Continues to Develop With Time

2A). At each follow-up point, no significant differences were observed between the two groups ($p > .05$). Compared with the preoperative level, Qmax appeared a significant improvement, whereas PVR significantly decreased (Figure 2B). In addition, no statistical differences were observed in these parameters between the two groups ($p > .05$). In general, postoperative Qmax, PVR, IPSS, and QoL appeared an ideal improvement during follow-up and almost reached the same level in both groups.

After catheter removal, SUI was observed in 27 patients (29.3%) in the conventional HoLEP group, whereas in HoLEP with mucosal sparing technique group was 17 (17.7%) ($p = .24$). During the follow-up, we found that some SUI recovered. There were six patients (6.5%) with long-term SUI (>12 months) in the conventional HoLEP group and one patient (1.0%) in the HoLEP with mucosal sparing technique group ($p < 0.01$). The difference is statistically significant. This statistical

Table 3. Comparison of Postoperative De Novo SUI Between Observation Group and Control Group.

	Observation group	Control group	*p* value
Immediate after catheter removal (*n*, %)	17 (17.7)	27 (29.3)	0.03
1 month (*n*, %)	11 (11.5)	16 (17.4)	0.24
3 month (*n*, %)	7 (7.3)	11 (11.9)	0.02
6 month (*n*, %)	2 (3.1)	8 (8.7)	<0.01
12 month (*n*, %)	1 (1.0)	6 (6.5)	<0.01

difference was similar at all follow-up points, except for the first month postoperation ($p = .24$) (Table 3).

Discussion

Although TURP was considered as the gold standard for surgical treatment of BPH in the past decades, various AEEPs have been developed and become popular options that replace TURP and open prostatectomy. Subsequently following technological improvement, HoLEP and other enucleation, such as bipolar, have been recommended as the first-line surgical therapies in BPH treatment (Karavitakis et al., 2019). Although HoLEP is considered a safe and effective surgical treatment, many urologists are still unfamiliar with it. A certain learning curve is required to achieve acceptable safety and efficacy for HoLEP (Kampantais et al., 2018).

In this study, we proved that HoLEP performed by an experienced urologist could be safe and effective when applied to BPH treatment. Compared with preoperative levels, IPSS and QoL decreased after operation in both groups. Thereafter, the PVR and Qmax also improved and remained satisfactory. In addition, the complication incidence was low in this cohort. HoLEP achieves ideal effects in terms of relieving LUTS, which may be due to its procedure being similar to open surgery; thus, enucleation is carried along the true anatomical plane between the outer peripheral zone and the inner hyperplastic adenoma. Meanwhile, enhanced coagulation property is another advantage of holmium laser, which contributes to reducing blood loss and decreasing transfusion rate during operation. This specialty has been demonstrated by many researchers (Cynk, 2014; Michalak et al., 2015) and is also indicated in our study. This preliminary result supports HoLEP as a definitive treatment for BPH patients

Although HoLEP can achieve better or at least equivalent outcomes than conventional TURP in treating patients with LUTS and urinary retention (Trotsenko et al., 2021), we must be conscious of the complications for HoLEP that includes SUI. SUI is the most relevant clinical outcome that was significantly affected by learning, although its transient nature is assuring (Elshal et al., 2017). De novo SUI after surgery is a common complication after HoLEP and previous follow-up data reported that early SUI occurred in 7.1% to 44.0% of patients after HoLEP (Cho et al., 2011; Houssin et al., 2021; Kobayashi et al., 2016). In general, the early postoperative de novo SUI rate (44 in 188, 23%) in our study was generally comparable with other reports regarding HoLEP. Although this SUI might be temporary, most of which ameliorate within 1 to 6 months, it induces anxiety and stress in the population during its duration. Thus, SUI is a state of distress that restricted the patient's QoL, in addition to extra-economic costs.

In this study, when all participants were divided into the conventional HoLEP group and HoEP with mucosal flap sparing technique group, interesting things were observed. Although, during postoperative follow-up, patients of both groups experienced similar recovery procedures, as delineated by Qmax, PVR, IPSS, and QoL, after adopting the new technique, the occurrence of short-term SUI was reduced. Although the SUI in both groups was ameliorating at each follow-up point, things in HoLEP with mucosal sparing technique group were better than in the conventional HoLEP group. However, this difference was not reflected in the postoperative QoL, which may be due to many factors. These results indicated that the new technique has advantages in the protection of urinary control functions and we tried to explain this phenomenon. During the anatomical enucleation of the prostate, the urethral mucosa and gland near the sphincter are completely removed, so that although the external sphincter can be constricted during the storage period, interlay is lacking within the closed ring structure, which causes an insufficient closure at this level and leads to SUI. However, the modified technique solves this problem well by preserving 1 cm mucosa and gland at the sphincter area. It did not only remove enough tissue that causes obstruction but also allows the urethra to be closed when the sphincter is contracted. Meanwhile, our data also identified that the new technique did not increase the operation time, bleeding, or other related complications.

Limitations

To some extent, several limitations of this article should be considered. First, the study included a limited number of cases in each group with limited information. Second, the follow-up period was relatively short for assessing the outcome of a benign disease. Third, this is a retrospective study and more rigorously designed randomized controlled study is needed to confirm the preliminary results. Fourth, as a useful functional assessment method, invasive urodynamic study was not routinely performed after surgery. Limitations aside, this study has some strengths worth mentioning, including rigorous design and well-validated assessments. To our knowledge, this is the first report that compares the modified urethral mucosal flap sparing HoLEP with the conventional HoLEP.

Conclusion

HoLEP could be an effective and safe treatment for BPH/LUTS. The efficacy was immediate and durable during follow-up. The use of the urethral mucosal flap sparing technique during HoLEP decreases the incidence of SUI without prolonging the operation time and increasing complications. This operation is an optional treatment for BPH and is safe and effective for clinical application.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethic Statement

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This research was approved by the Institutional Review Board of the First Affiliated Hospital of Nanjing Medical University (No. 2019-SR-138). All participants signed informed consent and the study was performed according to the Declaration of Helsinki (as revised in 2013).

ORCID iD

Pu Li https://orcid.org/0000-0002-3796-671X

Data Access Statement

The data sets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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