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Aquablation versus HoLEP: Propensity score matching analysis of functional outcomes and ejaculation preservation

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Purpose: This study aimed to compare the clinical outcomes of Aquablation and Holmium Laser Enucleation of the Prostate (HoLEP) for the treatment of benign prostatic hyperplasia (BPH), with emphasis on functional improvement, ejaculatory preservation, and perioperative safety.

Materials and Methods: We retrospectively analyzed data from January 2023 to March 2024, excluding patients with follow-up shorter than 3 months. Propensity score matching was performed using age, prostate volume, and preoperative prostate-specific antigen (PSA). Pre- and postoperative outcomes included International Prostate Symptom Score, Overactive Bladder Symptom Score, maximum flow rate (Qmax), post-void residual urine volume (PVR), PSA, and MSHQ-EjD (Male Sexual Health Questionnaire–Ejaculatory Dysfunction)-based ejaculatory grading (0–3). Paired t-tests, Wilcoxon signed-rank tests, McNemar's test, and Mann–Whitney U test were applied as appropriate.

Results: A total of 104 patients were included, with 34 matched pairs. Both procedures significantly improved lower urinary tract symptoms, with no significant differences in symptom score changes or PVR. HoLEP resulted in greater improvements in Qmax and PSA ($p=0.011$ and $p<0.001$, respectively). Aquablation demonstrated significantly better preservation of ejaculation ($p=0.002$). Although transient incontinence was more frequent in HoLEP and gross hematuria and urinary retention were more common in Aquablation, none of the complication rates showed statistically significant differences.

Conclusions: Aquablation and HoLEP are both effective surgical options for BPH. Aquablation offers comparable symptom relief with significantly superior ejaculation preservation, making it particularly suitable for sexually active patients. HoLEP provides greater deobstructive efficacy, as evidenced by superior Qmax and PSA outcomes. These findings support individualized, patient-centered decision-making.

Keywords: Aquablation; Benign prostatic hyperplasia; Transurethral resection of prostate

INTRODUCTION

Benign prostatic hyperplasia (BPH) is a common condition that causes lower urinary tract symptoms (LUTS) in adult men [1]. The gold standard for the surgical management of BPH has long been transurethral resection of the prostate (TURP). Holmium Laser Enucleation of the Prostate (HoLEP) is also considered another gold standard

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due to its high deobstructive efficacy achieved via complete enucleation of the prostate adenoma [2,3]. However, TURP and HoLEP, while effective and proven procedures, have the disadvantage of longer surgical times in cases of large prostate volume. They also carry risks of bleeding and sexual side effects such as retrograde ejaculation. As a novel alternative to TURP, minimally invasive surgeries (MIS) for BPH are being introduced to reduce surgical time and minimize complications [4,5]. Among them, Aquablation is a surgical technique that utilizes a robotic waterjet system [6]. Using a "windshield wiper" motion, the prostate apex can be preserved to minimize damage to the ejaculatory pathway. Aquablation has proven effective for obstructive BPH; however, data comparing its efficacy, safety, and ejaculation preservation to HoLEP are still limited [7-9]. In this study, we analyzed the initial 1-year clinical data on Aquablation. We compared these findings with those of HoLEP from the same period to assess functional outcomes and the efficacy of Aquablation in ejaculatory preservation using propensity score matching (PSM) analysis.

MATERIALS AND METHODS

1. Ethics statement

The study was conducted according to the guidelines of the Declaration of Helsinki (2013), and approved by the Institutional Review Board (IRB) of Yonsei University College of Medicine (approval number: 4-2024-1490). The IRB of Yonsei University College of Medicine waived the requirement of obtaining informed consent since this study retrospectively reviewed anonymous patient data and did not include the use of human tissue samples.

2. Study populations and parameters

We retrospectively analyzed Aquablation and HoLEP clinical data from January 1, 2023 to March 31, 2024, using data available up to November 30, 2024. Cases were excluded if the follow-up period was less than 3 months or if other etiologies—such as neurogenic bladder—could cause LUTS apart from bladder outlet obstruction. All patients underwent a preoperative pressure-flow study to evaluate for bladder outlet obstruction. Patients with clinically apparent neurogenic diseases were excluded. In cases where low-pressure, low-flow patterns were observed, a urodynamic study and cystoscopy were performed to confirm bladder outlet obstruction before surgery. The clinical data included age, prostate volume, and pre and postoperative measures: the International Prostate Symptom Score (IPSS), quality of life score of the IPSS (LQ), Overactive Bladder Symptom Score (OABSS), maximum flow rate (Qmax), post-void residual urine volume (PVR), and the Male Sexual Health Questionnaire–Ejaculatory Dysfunction (MSHQ-EjD). Postoperative data were collected at the final outpatient clinic follow-up visit for each patient. Although variability in follow-up timing existed among patients, comparative analysis was performed to ensure that differences in follow-up duration between the Aquablation and HoLEP groups did not significantly affect the results. To compare Aquablation and HoLEP, each parameter was assessed by calculating the difference between preoperative and postoperative values (Delta-IPSS, Delta-LQ, Delta-OABSS, Delta-Qmax, and Delta-PVR).

3. Surgical methods

The HoLEP procedure was performed using a Lumenis Pulse™ 120H Holmium Laser System with MOSES™ Technology (Lumenis Ltd.) by a single surgeon with over 15 years of HoLEP experience. HoLEP procedures were performed using the standard three-lobe enucleation technique. No specific ejaculation-sparing modifications were applied during surgery [10]. Aquablation was performed using the AquaBeam Robotic System (PROCEPT BioRobotics), with the first case conducted in May 2023. Aquablation was also performed by the same surgeon as HoLEP. In all Aquablation cases, two sessions of waterjet ablation were performed to achieve sufficient adenoma removal while preserving the anterior prostate and minimizing damage to the external sphincter. In Aquablation procedures, a verumontanum protection zone was planned by maintaining an approximate 1-cm safety margin from the verumontanum. This contouring strategy was based on prior studies suggesting that preserving this anatomical region is critical for optimizing postoperative ejaculatory function [11]. Since the tissue resected by aquablation is not available for pathology, a prostate biopsy was performed prior to surgery in patients with prostate-specific antigen (PSA) elevation to exclude prostate cancer. In Aquablation, fluffy tissue resection and bleeding control were carried out after waterjet ablation using the OES Pro Resectoscope (Olympus Corp.). All preoperative alpha-blockers and 5-alpha reductase inhibitors were discontinued after surgery. Postoperatively, continuous bladder irrigation was maintained until the day before discharge, and urethral catheter removal was performed on the day of discharge. Hospital stay duration was recorded for all patients.

4. Measuring ejaculation preservation

The MSHQ-EjD questionnaire was administered only to patients who were sexually active before surgery and had agreed to complete the survey among those who underwent

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Aquablation and HoLEP. Patients who exhibited anejaculation preoperatively were excluded from the ejaculation preservation analysis to minimize confounding effects from reversible drug-induced ejaculatory dysfunction. The analysis was restricted to patients with preserved ejaculatory function before surgery to more accurately assess the surgical impact on ejaculation. Patients who experienced anejaculation before surgery were excluded from the ejaculation preservation analysis. Patients were advised to resume intercourse starting 2 months post-surgery, and MSHQ-EjD results were compared based on the scores at their last outpatient visit. Patients were classified into four groups based on changes in MSHQ-EjD scores before and after surgery, collectively referred to as the EjQ groups. The classifications were as follows: Grade 1 (anejaculation), Grade 2 (decreased; a reduction of more than 20% compared to the preoperative score), Grade 3 (no change; a variation of less than 20% from the preoperative score), and Grade 4 (increased; an improvement of more than 20% compared to the preoperative score).

5. Postoperative complications

Postoperative complications were collected and classified according to the Clavien–Dindo classification system. During follow-up, if patients exhibited symptoms such as dysuria or a worsening weak urinary stream, cystoscopy was performed to diagnose urethral stricture, bladder-neck contracture, prostatic fossa calcification, or stone formation.

6. Statistical analysis and subgroup analysis

The characteristics of each patient were investigated using descriptive statistics. PSM was performed using the R version 4.4.1 (R Core Team, 2024), employing the nearest-neighbor matching method. Covariates included age at the time of surgery, PSA, and prostate volume. Covariate balance after PSM was assessed using both p-values and standardized mean differences (SMDs). An SMD less than 0.1 was considered indicative of good balance between groups. Variables matched included age, prostate volume, and PSA. Although PSM was employed, minor residual imbalances were noted, which have been discussed as limitations.

After PSM, continuous variables were compared using paired t-tests for normally distributed data and Wilcoxon signed-rank tests for non-normally distributed data. No adjustment for multiple comparisons was performed, as analyses were focused on pre-specified primary outcomes. For ejaculation preservation, patients were categorized into EjQ subgroups. Since this subgroup did not maintain the matched-pair structure, and the outcome was ordinal, the Mann–Whitney U test was used to compare grades between the Aquablation and HoLEP groups. Postoperative complication rates were compared using McNemar's test, which is appropriate for categorical data in matched-pair designs following PSM. A post-hoc power analysis was conducted for the primary comparative outcomes using the observed effect sizes and sample sizes after PSM. Statistical power was calculated based on a two-sided significance level of 0.05.

RESULTS

A total of 104 patients were included in the study during the research period, 34 in the Aquablation group and 70 in the HoLEP group. PSM was performed using age at operation, prostate volume, and preoperative PSA as covariates, resulting in matched data of 34 patients in each group (Aquablation: n=34, HoLEP: n=34). Table 1 summarizes the covariate balance after PSM. PSA values were well balanced (SMD=0.012), prostate volume showed moderate balance (SMD=0.315), while age exhibited some residual imbalance (SMD=0.532).

The mean age for the Aquablation group was 62.2±6.1

Table 1. Demographics of patients

	Aquablation (n=34)	HoLEP (n=34)	p-value	SMD
Age (y)	62.2±6.1	65.4±5.9	0.017[a]*	0.532
Prostate volume (g)	76.2±46.1	64.7±23.2	0.761	0.315
PSA (ng/mL)	5.5±4.8	5.5±4.0	0.761	0.012
Follow-up duration (mo)	9.6±4.4	11.4±4.7	0.064[a]	
Operation time (min)	87.6±35.6	99.6±31.6	0.091	
Hospital stay after operation (d)	2.09±0.45	2.03±0.17	0.414	

Values are presented as mean±standard deviation.

HoLEP, Holmium Laser Enucleation of the Prostate; SMD, standardized mean difference; PSA, prostate-specific antigen.

[a]:This variable satisfied the normality assumption and was analyzed using a paired t-test, while the remaining variables did not meet the normality assumption and were analyzed using the Wilcoxon signed-rank test.

*p<0.05.

Table 2. Functional outcomes of Aquablation and HoLEP

		Preoperative data	Postoperative data	p-value
Aquablation (n=34)	IPSS	22.4±5.2	9.1±4.3	<0.001*
	LQ	4.7±0.7	1.7±0.9	<0.001*
	OABSS	6.9±2.8	3.7±2.6	<0.001*
	Qmax	9.8±4.7	19.4±8.0	<0.001*
	PVR	72.9±67.8	30.5±30.2	<0.001*
	PSA	5.5±4.8	5.0±4.3	0.057
HoLEP (n=34)	IPSS	20.5±5.8	8.2±5.5	<0.001*
	LQ	4.4±0.7	1.6±1.2	<0.001*
	OABSS	5.9±3.4	3.7±2.3	0.002*
	Qmax	8.4±3.6	22.9±7.7	<0.001*
	PVR	107.3±108.3	20.4±23.6	<0.001*
	PSA	5.5±4.0	1.1±1.0	<0.001*

Values are presented as mean±standard deviation.
HoLEP, Holmium Laser Enucleation of the Prostate; IPSS, International Prostate Symptom Score; LQ, quality of life score of the IPSS; OABSS, Overactive Bladder Symptom Score; Qmax, maximum flow rate; PVR, post-void residual urine volume; PSA, prostate-specific antigen.
*p<0.05.

Table 3. Comparative analysis between HoLEP and Aquablation

Delta-variable[a]	Aquablation (n=34)	HoLEP (n=34)	p-value
Delta-IPSS	-13.3±6.3	-12.4±7.9	0.563[b]
Delta-LQ	-2.9±1.2	-2.8±1.3	0.650
Delta-OABSS	-3.2±3.3	-2.3±4.0	0.317[b]
Delta-Qmax	9.6±6.3	14.5±8.6	0.011[b]*
Delta-PVR	-42.3±63.5	-87.0±101.9	0.104
Delta-PSA	-0.8±2.2	-4.4±3.5	<0.001*

Values are presented as mean±standard deviation.
HoLEP, Holmium Laser Enucleation of the Prostate; IPSS, International Prostate Symptom Score; LQ, quality of life score of the IPSS; OABSS, Overactive Bladder Symptom Score; Qmax, maximum flow rate; PVR, post-void residual urine volume; PSA, prostate-specific antigen.
[a]:Delta-variable=(postoperative variable)-(preoperative variable)
[b]:This variable satisfied the normality assumption and was analyzed using a paired t-test, while the remaining variables did not meet the normality assumption and were analyzed using the Wilcoxon signed-rank test.
*p<0.05.

years, and the mean follow-up duration was 9.6±4.4 months. For the HoLEP group, the mean age was 65.4±5.9 years, and the mean follow-up duration was 11.4±4.7 months. The mean operative time was significantly shorter in the Aquablation group compared to the HoLEP group (87.6±35.6 minutes vs. 99.6±31.6 minutes, p=0.091). The mean hospital stay after operation was 2.09±0.45 days in the Aquablation group and 2.03±0.17 days in the HoLEP group. No statistically significant difference was observed between the groups (p=0.414). There was no statistically significant difference in follow-up duration between the two groups (p=0.064), indicating minimal risk of bias related to timing differences. Patient characteristics are presented in Table 1.

The pre- and postoperative data for Aquablation and HoLEP, along with their comparative analysis, are shown in Table 2. Both surgical methods demonstrated significant improvements in IPSS, LQ, OABSS, Qmax, and PVR. However, the change in PSA did not reach statistical significance in the Aquablation group (p=0.057).

The differences in pre- and postoperative data were analyzed to compare Aquablation and HoLEP, and the results are shown in Table 3. When comparing delta values between Aquablation and HoLEP, there were no significant differences in delta IPSS, LQ, OABSS, or PVR (p=0.563, p=0.650, p=0.317, and p=0.104, respectively). However, Delta-Qmax was significantly higher in the HoLEP group (p=0.011), and the reduction in PSA levels was significantly greater in the HoLEP group (p<0.001). The post-hoc power analysis revealed that the effect size (Cohen's d) for the change in Qmax was 1.25, with a resulting statistical power exceeding 99.9% (α=0.05). This indicates sufficient sensitivity to detect meaningful differences between groups despite the relatively small sample size.

In terms of ejaculation preservation, the patients who were sexually active before surgery and completed the survey included 22 in the Aquablation group and 16 in the HoLEP group. Considering the presence or absence of ejaculation (grades 2–4), 77.3% of patients in the Aquablation group retained ejaculation compared to 43.8% in the HoLEP group. Regarding the proportion of patients maintaining or improving ejaculation grades (grades 3–4) compared to

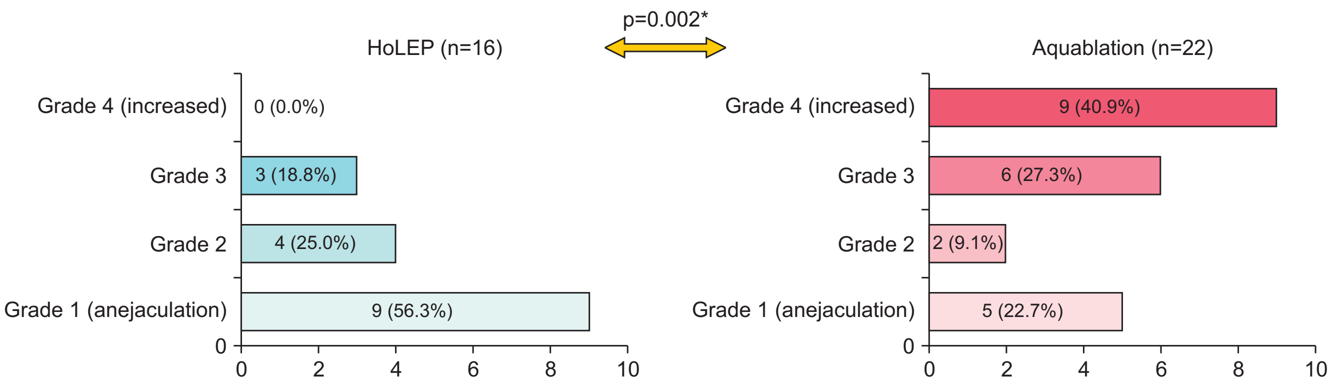
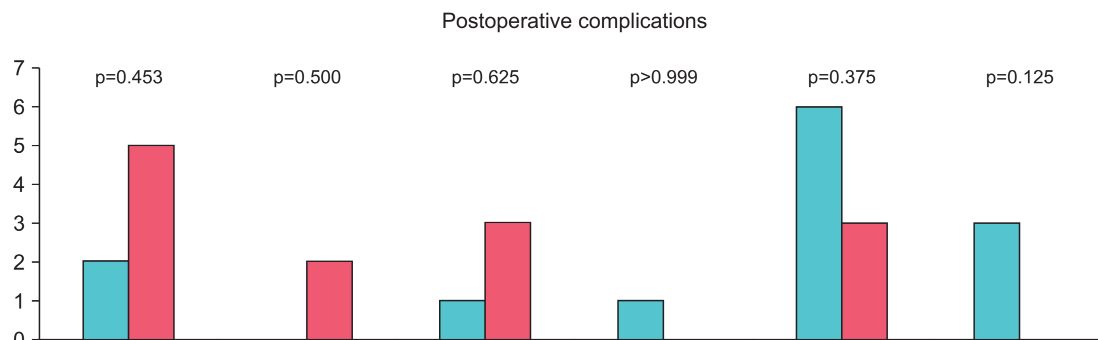


Fig. 1. Ejaculation preservation outcomes of HoLEP and Aquablation. Ejaculation preservation was assessed only preoperatively in sexually active patients and classified into four grades using the Male Sexual Health Questionnaire–Ejaculatory Dysfunction (MSHQ-EjD): Grade 1 (anejaculation), Grade 2 (decreased; >20% decrease in score), Grade 3 (no change), and Grade 4 (increased; >20% increase in score). Preservation was defined as Grade 3+Grade 4. This analysis was conducted on participants who were sexually active before surgery and agreed to complete the MSHQ-EjD questionnaire. HoLEP, Holmium Laser Enucleation of the Prostate. *p<0.05.



	Gross hematuria	Urinary retention	Prostatic fossa calcification	Bladder neck contracture	*De novo* OAB	Transient incontinence
HoLEP (n=34)	2	0	1	1	6	3
Aquablation (n=34)	5	2	3	0	3	0

Fig. 2. Postoperative complications of HoLEP and Aquablation. HoLEP, Holmium Laser Enucleation of the Prostate; OAB, overactive bladder.

preoperative status, the rates were 68.2% in the Aquablation group and 18.8% in the HoLEP group, with significant differences by Mann–Whitney U test (p=0.002). These findings are demonstrated in Fig. 1.

Postoperative complications for both HoLEP and Aquablation are presented in Fig. 2. None of the postoperative complications showed statistically significant differences between the two groups. Transient incontinence was more frequently observed in the HoLEP group, but this difference was not statistically significant according to McNemar's test (p=0.125). Bladder neck contracture and *de novo* OAB also occurred more often in the HoLEP group, whereas gross hematuria, urinary retention, and prostatic fossa calcification were more common in the Aquablation group. All cases of transient incontinence resolved within 6 months postoperatively, and no patients had persistent incontinence. In cases of *de novo* OAB symptoms, the beta-3 agonist was prescribed, and symptoms returned to preoperative levels after 3 months of treatment and discontinuation of the medication.

DISCUSSION

With the rise of MIS for BPH, the options for surgical management of BPH have become more diverse and complex. Treatment should move beyond the gold standard to a patient-tailored approach. Shared decision-making has a significant impact on patient satisfaction and overall outcomes [12]. When choosing an appropriate surgical method, various factors must be considered. These include prostate volume and anatomical features, such as intravesical prostatic protrusion and median lobe hypertrophy. Individual patient needs, including preferences for noninvasive treatment or desire for ejaculation preservation, should also be assessed. When patients are unable or unwilling to take medication due to side effects, MIS may be a favorable treatment option before TURP or HoLEP [13]. The next step in BPH treatment guidelines should be shared decision-making with patients. Furthermore, the patient's economic circumstances are an important consideration. In this regard, comparing HoLEP and Aquablation could help clarify the strengths and weaknesses of these procedures, aiding in the optimal choice for the patient.

The most important finding of this study is that the change in symptom questionnaire scores showed no significant difference between Aquablation and HoLEP. At the same time, HoLEP demonstrated superiority in Qmax and PSA decrease, and Aquablation showed superiority in ejaculation preservation. HoLEP, which utilizes a Holmium laser to achieve near-complete enucleation of the adenoma, is known to be the most effective method for deobstruction to date [14]. In particular, one prospective study reported that even in cases of chronic urinary retention, HoLEP showed better outcomes compared to TURP or open prostatectomy [15]. In contrast, the primary aim of Aquablation is to efficiently resect only a portion of the adenoma via a wedge-resection technique, preserving non-obstructive zones such as the anterior lobe. This less extensive resection inherently results in lower deobstructive efficacy, which may explain the relatively smaller improvements in Qmax and PSA reduction observed in this study. Although resection volume was not directly measured, prior reports have consistently shown that PSA decreases are less pronounced following Aquablation than after complete enucleation techniques [16]. Nonetheless, despite its more conservative tissue removal, Aquablation achieved comparable symptom relief and was associated with high patient satisfaction. In addition, although not statistically significant, the shorter operative time observed with Aquablation may reflect the procedural efficiency conferred by its robotic, automated tissue resection. This may support faster intraoperative workflow and reduced manual dissection, especially in patients without large anterior adenomas.

In the present study, none of the postoperative complications demonstrated statistically significant differences between the Aquablation and HoLEP groups when analyzed using McNemar's test. While transient incontinence occurred more frequently in the HoLEP group, this difference did not reach statistical significance ($p=0.125$). Similarly, bladder neck contracture and *de novo* OAB were more commonly reported in the HoLEP group. In contrast, gross hematuria, urinary retention, and prostatic fossa calcification were more frequently observed in the Aquablation group. Although these differences were not statistically significant, they may reflect the differing anatomical and technical characteristics of each procedure. Larger studies with sufficient power are warranted to determine whether these trends are clinically significant.

Although the follow-up duration in our study was limited to approximately 9 to 12 months, previous long-term studies of HoLEP have demonstrated that greater improvements in Qmax and PVR are associated with durable symptom control over 5 years or longer. Similarly, while long-term sexual satisfaction data specifically following Aquablation are still emerging, preservation of antegrade ejaculation has been shown to positively influence sexual satisfaction and quality of life in men undergoing BPH surgery. Future prospective studies with extended follow-up are necessary to confirm the long-term clinical benefits of both procedures.

In terms of ejaculation preservation, Aquablation was found to be superior. The rate of patients who maintained at least postoperative partial ejaculation, excluding cases of anejaculation, was approximately 80%. The proportion of cases where postoperative ejaculation was maintained at or above preoperative levels (grade 3 or higher) was about 67%. In contrast, for HoLEP, only 19% of patients reached grade 3, and the rate of anejaculation was 56%. Ejaculation significantly impacts men's quality of life regardless of age [17]. It is closely associated with sexual enjoyment and satisfaction in both men and women, while anejaculation can reduce orgasm [18]. Therefore, for patients who wish to preserve ejaculation but require resective surgery, Aquablation presents a more favorable option compared to HoLEP. The relatively lower ejaculation preservation rate observed in the Aquablation group compared to previous reports may be partly attributed to the surgeon's learning curve with the Aquablation procedure. Moreover, our study employed the EjQ grading system, which enabled a more detailed and rigorous assessment of ejaculatory function changes, rather than a simple dichotomous evaluation. These factors may have contributed to differences in reported outcomes.

This study is significant in that it does not merely investigate whether ejaculation preservation is achieved but classifies and examines the quality of ejaculation. The exact mechanism by which Aquablation preserves ejaculation is not clearly understood. Aquablation involves wedge resection to excise the prostatic adenoma while preserving the anterior part. Additionally, it conserves the prostate apex and areas around the verumontanum. Attempts and studies on ejaculatory duct-preserving TURP have also been conducted in the past. Several research teams have studied ejaculation-preserving TURP, and although the detailed surgical techniques differ among them, the underlying prin-

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ciple has been the preservation of the ejaculatory duct near the verumontanum. All studies have concluded that ejaculation preservation is superior to conventional TURP [19-21]. It is also speculated that in Aquablation, ejaculation can be preserved by using the apical sparing technique or Butterfly technique around the apex near the verumontanum to protect the ejaculatory duct.

From the perspective of long-term functional outcomes, Aquablation is inherently associated with a smaller adenoma resection volume compared to HoLEP, which raises potential concerns about its long-term functional results. Despite these concerns, Aquablation has demonstrated significant improvements in urinary symptoms, and the long-term results reported to date have been favorable [22,23]. The longest available outcome data for Aquablation are the 5-year follow-up results from the WATER II study [22,23]. However, data beyond this timeframe are not yet available. To enable a thorough comparison of long-term outcomes, further research is necessary to investigate Aquablation's performance beyond 5 years, including retreatment rates and sustained efficacy.

This study has several limitations. First, its retrospective, single-center design may introduce inherent bias and limit the generalizability of the findings. Second, the short follow-up duration precludes assessment of long-term outcomes. Third, all procedures were performed by a single surgeon with extensive experience in HoLEP but limited exposure to Aquablation, introducing a potential learning curve effect. Fourth, there was variability in follow-up timing; however, no significant difference was observed between groups, suggesting minimal bias. Fifth, although PSM was applied, a residual imbalance in age remained, reflecting the limitations of nearest neighbor matching without caliper constraints. Lastly, patients with preoperative anejaculation—possibly related to reversible alpha-blocker effects—were excluded from the ejaculation preservation analysis. While this helped isolate the surgical impact, it may have excluded patients with medication-related dysfunction.

Nevertheless, this study offers valuable insights by employing PSM to compare HoLEP and Aquablation under standardized conditions directly. This approach minimizes confounding variables and allows for a more accurate assessment of the relative strengths and weaknesses of each procedure. Future studies with larger sample sizes, multicenter involvement, and extended follow-up durations are warranted to provide a more comprehensive understanding of the comparative effectiveness of these two surgical modalities. The findings underscore the need for continued research into the long-term functional outcomes and retreatment rates associated with Aquablation, as well as its potential role as a patient-preferred, ejaculation-preserving option for BPH management.

CONCLUSIONS

Aquablation and HoLEP are both effective treatments for BPH, with no significant differences in symptom score improvement. However, Aquablation offers superior preservation of ejaculation, a critical factor for quality of life. This advantage makes it particularly appealing to patients who prioritize sexual function and overall recovery. On the other hand, HoLEP demonstrates better outcomes regarding Qmax improvement, suggesting it may have superior deobstruction efficacy. Therefore, during shared decision-making with patients, it is essential to explain these differences and determine the surgical method accordingly. Further research incorporating long-term follow-up data is necessary to validate these findings.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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AUTHORS' CONTRIBUTIONS

Research conception and design: Jang Hwan Kim and Kyung Tak Oh. Data acquisition: Kyung Tak Oh. Statistical analysis: Kyung Tak Oh. Data analysis and interpretation: Kyung Tak Oh. Drafting of the manuscript: Kyung Tak Oh. Critical revision of the manuscript: Jang Hwan Kim. Supervision: Jang Hwan Kim. Approval of the final manuscript: all authors.

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