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BENIGN PROSTATIC HYPERPLASIA (K MCVARY, SECTION EDITOR)

A Systematic Review of Reported Ejaculatory Dysfunction in Clinical Trials Evaluating Minimally Invasive Treatment Modalities for BPH

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Abstract

Purpose of Review To explore the sexual outcomes following the novel minimally invasive surgical procedures for benign prostatic hyperplasia- (BPH-) related lower urinary tract symptoms (LUTS), with an emphasis on ejaculatory dysfunction (EjD).

Recent Findings A database search with a 10-year time restriction was carried out until February 20, 2020 using MEDLINE through the PubMed Platform evaluating minimally invasive treatment modalities for BPH and their effect on EjD. After the article selection, we retrieved data for men randomized in 19 different studies with results in 40 separate published articles investigating minimally invasive BPH surgery and reporting EjD rates. To date, water vapor thermal therapy or Rezūm, prostatic urethral lift (PUL) or UroLift®, prostate artery embolization (PAE), and Aquablation showed acceptable rates (< 2%) of retrograde ejaculation by 1 year and had very low adverse events related to the procedure. Both PUL and Rezūm demonstrated lower rates when compared with PAE and Aquablation.

Summary With comparable sexual side effect profiles postoperatively, clinicians may determine which therapeutic modality is optimal for patients based on efficacy and cost-benefit. Further randomized clinical trials are required to directly compare the effect of novel minimally invasive surgical procedures for BPH-related LUTS on ejaculation and sexual function.

Keywords Ejaculatory dysfunction · Benign prostatic hyperplasia · Water vapor thermal therapy · Prostatic urethral lift · Prostate artery embolization · Aquablation

Introduction

Benign prostatic hyperplasia (BPH) is a benign proliferation of the tissue in the transition zone of the prostate. The prevalence of BPH increases with age with autopsy studies showing histological prevalences of 8, 50, and 80% in the fourth, sixth, and ninth decades of life, respectively [1, 2]. The gold standard treatment of BPH is the transurethral resection of the prostate (TURP). Unfortunately, men who undergo TURP have considerable sexual dysfunction, including retrograde ejaculation (RE). Up to 66.1% of men who undergo TURP report RE [3]. RE will also affect three out of four men treated with Holmium laser enucleation of the prostate (HoLeP) [4].

In the last several decades, multiple treatments have been introduced for the treatment of BPH to not only treat lower urinary tract symptoms (LUTS) (Fig. 1) but also have potentially fewer sexual side effects. RE occurs when the sphincter of the bladder neck fails to contract causing the semen to reflux into the urinary bladder. RE often occurs after BPH treatments which do not preserve or affect the bladder neck. This may be avoided in treatments which do not directly affect the bladder neck, such as novel minimally invasive techniques.

With a modern emphasis on improved quality of life in patients suffering from BPH, there has been an impetus to develop ejaculatory-preserving minimally invasive techniques. The present systematic review aimed to explore the sexual side effects of these novel minimally invasive surgical procedures for BPH-related LUTS, with an emphasis on EjD.

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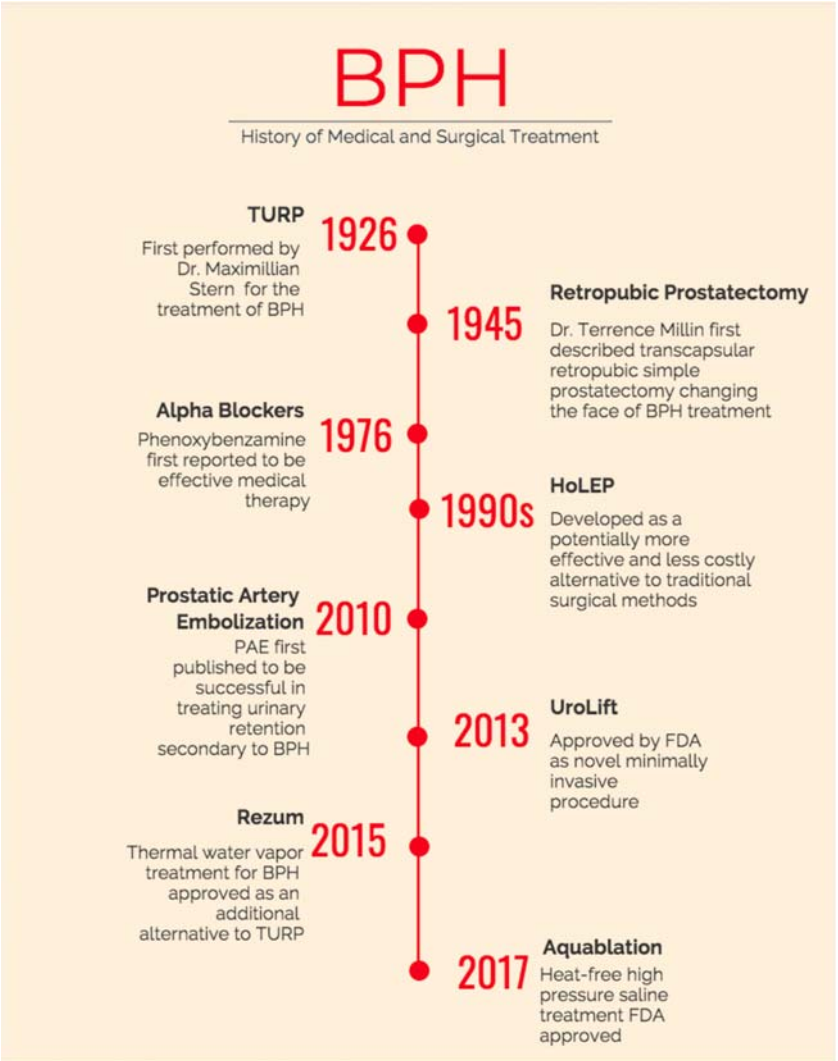

Fig. 1 History of medical and surgical treatment for BPH

Search Strategy

A database search with a 10-year time restriction was carried out until February 20, 2020 using MEDLINE through the PubMed Platform. After consensus among all the authors, the following search terms were used and pooled together in each subgroup with the Boolean operator "OR:" "Prostatic hyperplasia," "LUTS," and "lower urinary tract symptoms" to identify studies regarding LUTS; "UroLift®," "Prostatic Urethral Lift," "PAE," "prostate artery embolization" and "prostatic artery embolization," "Rezūm" and "transurethral water vapor therapy," "aquablation," and "aquabeam" for studies regarding surgical techniques used for LUTS treatment; "ejaculation," "anejaculation," "retrograde ejaculation," "painful ejaculation," "ejaculatory dysfunction," and "sexual dysfunction" for studies investigating or at least reporting information on the ejaculatory function (EjF) [3]. The three subgroups were then pooled together with the Boolean operator "AND," leading to a total of 520 identified records. The search process was carried out according to the PRISMA criteria and is shown in Fig. 2. The minimum criteria for the inclusion were the rate of EjD and the period of assessment in relation to when the surgery was carried out. Papers reporting the follow-up data on studies already included were excluded, unless they reported relevant additional information on the EjD rates [3]. Two authors (SDL, DV) independently screened all the abstracts identifying a total of 104 abstracts and 40 articles. The disagreement on the inclusion of a paper was resolved by a consultation among the senior authors (TFNL, RR).

Evidence Synthesis Methodology, Outcome Measures, and Limitations

We retrieved the data for men randomized in 19 different studies with results in 40 separate published articles investigating minimally invasive BPH surgery and reporting EjD

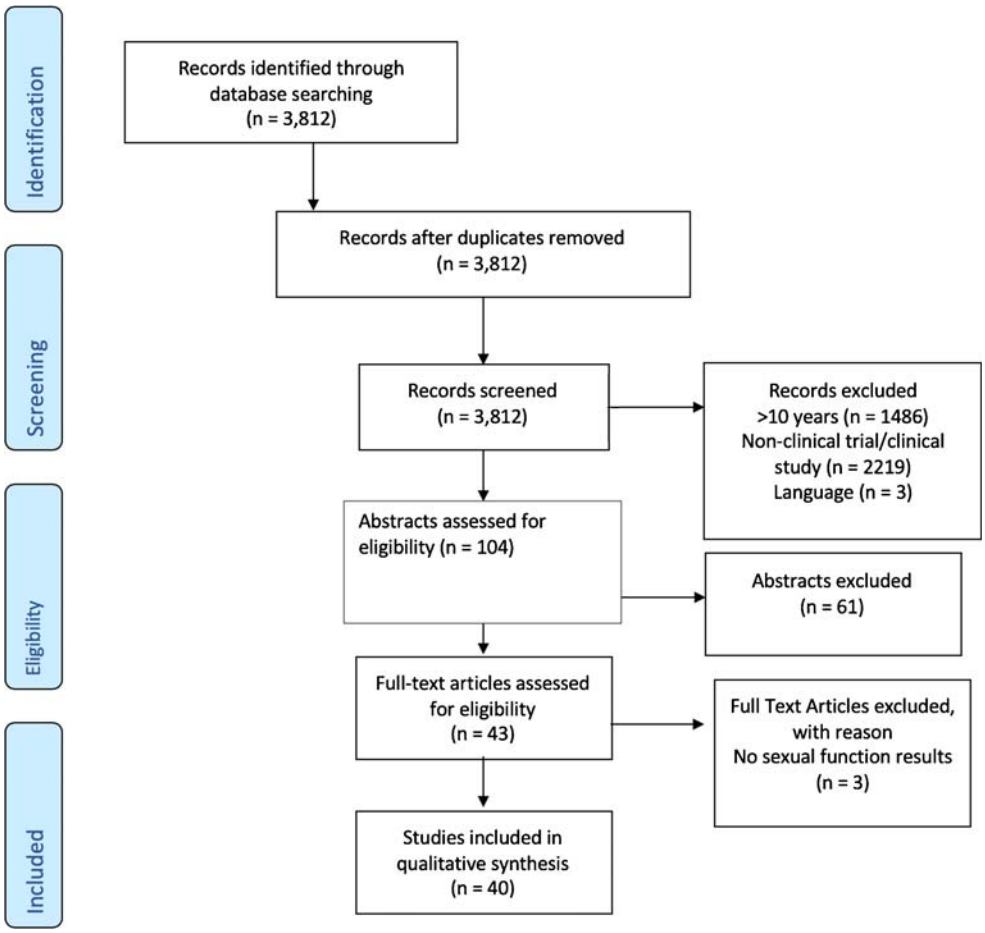

Fig. 2 PRISMA flow diagram. From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6 (7): e1000097. doi:10.1371/journal.pmed1000097

rates. Three studies assessed EjD as a primary outcome, 2 prostatic urethral lift (PUL) [5, 6], and 1 water vapor thermal energy study [7]. EjD was either studied independently or as a potential adverse event. The definition of "ejaculatory dysfunction" was not standardized, and in the vast majority of the studies, EjD or RE was described as a function of the international index of erectile function (IIEF) score. A total of 8 articles reported results from 2 PUL clinical trials [5, 6, 8–13]. For Rezūm, 7 articles describing the results from 2 clinical trials were included [7, 14–18]. Eleven articles reporting the results of 4 clinical trials on Aquablation were included [19, 20, 21•, 22–25, 26••, 27, 28]. PAE was investigated in 11 trials with 14 articles exploring the results [29–37, 38•, 39–42]. The inclusion criteria generally required men with BPH who had LUTS-related symptoms, an IPSS ≥ 12–13, a Qmax of < 15 mL/s, and generally an age group of 45 to 80 years of age, although there were variations among the trials. A few studies focused or reported separate results on prostates of certain size especially larger (> 80 g) prostates ($n = 4$). The exclusion criterion was generally those patients with significant co-morbidities and uncontrolled chronic diseases such as diabetes.

The 19 included trials are summarized in Table 1. Of the 19 trials, only 10 had readily available information on the national clinical trial registry. The majority of the included trials included a study period ($n = 17$). Seven of the trials included cohorts with more than 100 patients, with only a few including less than 20 ($n = 4$). The majority of the trials had median/mean follow-up of 12 months or more ($n = 14$). Four trials compared these novel modalities directly with TURP in matched patient cohorts. Almost all of the trials reported the results of changes in the Male Sexual Health Questionnaire (MSHQ) or IIEF scores ($n = 16$). All trials reported adverse events.

Surgical Treatments

Water Vapor Thermal Therapy

Water vapor thermal therapy with the Rezūm™ System (Rezūm System, Boston Scientific, Marlborough, MA) uses thermal energy in the form of water vapor, delivered by convection, to ablate obstructive prostatic tissue [15]. Due to the convective properties of water, a large amount of stored thermal energy is able to be transferred transurethrally (540 cal/mL H_2O). The technology works by steam or vapor entering through the spaces between cells to the tissue plane boundaries in between the prostate zones, thereby disrupting cell

Table 1 Minimally invasive surgical procedures for BPH, including sexual results and adverse events

Modality	Study	Study period	Cohort	Median/ mean fu time	Sexual results	Adverse events
Urolift	NCT01294150. L.I.F.T. Study: RCT/Sham	02/2011–12/2014	206: 140 UroLift, 66 Sham	12 mo, 2 yrs, 3 yrs, 4 yrs, 5 yrs	Change in MSHQ-EjD vs baseline: [3 mo + 2.3 ± 2.6, 12 mo + 1.6 ± 2.7, 2 yrs + 1.1 ± 2.5, 3 yrs + 0.6 ± 2.5, 4 yrs + 0.8 ± 2.4, 5 yrs + 1.56] $P < 0.0001$. MSHQ-EjD bother $P < 0.0001$ all fu time. Change in SHIM score vs baseline: [3 mo + 1.3, 12 mo + 0.7, 2 yrs + 1.1, 3 yrs + 0.5, 4 yrs + 0.3]. IIEF-5 change sig only 24 mo.	Pelvic pain/discomfort (21%). No sig difference from SHAM (2.71 and 2.67 out of 10, respectively; $P = 0.9$). No incidence of de novo, sustained ED or retrograde Ej.
	NCT01533038. BPH6 study: RCT/TURP	02/2012–10/2013	80: 45 PUL, 35 TURP	12 mo and 2 yrs	Change in MSHQ-EjD vs baseline: [3 mo + 0.7 ± 3.9, 6 mo + 1.1 ± 2.4, 12 mo + 1.3 ± 3.3, 2 yrs + 0.3 ± 3.4]. Comparison $P < 0.001$. Change in MSHQ-EJD bother comparison insig. Change in SHIM score compared to baseline at each time interval: [3 mo − 0.7 ± 5.2, 6 mo − 0.5 ± 4.4, 12 mo − 0.1 ± 4.7, 2 yrs− 0.2 ± 4.3] insig comparison p.	No sexual adverse events
Rezum	NCT01912339: Prospective	09/2013–08/2017	136: 77 at 12 mo, 71 at 2 yrs, 63 at 3 yrs, 58 at 4 yrs	3 mo, 12 m-o, 3 yrs, 4 yrs	Change in MSHQ-EjD vs baseline: [3 mo + 0.3 ± 4.3, 12 mo − 0.3 ± 3.5, 2 yrs − 0.5 ± 4.2, 3 yrs − 1.4 ± 3.8 ($P = 0.0046$), 4 yrs − 1.8 ± 4.4 ($P = 0.0038$)]. Change in IIEF-EF score vs baseline [3 mo + 0.1 ± 7.4, 12 mo − 0.3 ± 7.5, 2 yrs − 1.2 ± 7.6, 3 yrs − 2.0 ± 8.2, 4 yrs − 2.5 ± 8.7 ($P = 0.0333$)]	No sexual adverse events
	Rezum Dixon et al.	Not known	65	1 yr	IIEF (3 mo data) baseline: 32.5 (25.2), 3 mo: 38.6 (24.3). IIEF (1 yr data) baseline: 33.4 (25.1), 12 mo 33.4 (25.1)	No sexual adverse events
Aquablation	NCT02505919 WATER	10/2015–12/2016	184: 117 Aqua/ 67 TURP	12 mo	6 mo anEj Aqua vs TURP (10 vs 36%, $P = 0.0003$) Aqua anEj when posttreatment cautery was avoided (7 vs 16%, $P = 0.2616$). Change MSHQ-EjD or IIEF-5 scores in 33% Aqua and 56% TURP ($P = 0.0268$). Sex active men mean EF scores on IIEF-15 stable after Aqua vs decrease TURP. Overall sex satisfaction Aqua sig better ($P = 0.0492$). Ej function scores on MSHQ-EjD stable after Aqua but sig worse after TURP ($P = 0.0254$). In prostate > 50 g anEj at 6 mo after Aqua vs TURP (2 vs 41%, $P = 0.0001$)	6 mo: CD grade 1 sexual (retrograde Ej): 8 vs 16 $P = 0.0012$. Among sexually active subjects, the rate of anEj was lower in pts. treated with Aqua than TURP (9 vs. 45%, respectively, $P = .0006$). 12 mo: Retrograde Ej 1 (0.9%) for Aqua 2 (3.1%) for TURP $P = 0.2932$ Sexual dysfunction 0 for Aqua 1 (1.5%) for TURP ($P = 0.3591$)
	NCT03123250. WATERII	9/2017–12/2017	101	12 mo	MSHQ-EjD 8.1 (95% CI: 7.2–9.0) at baseline to 7 (5.8–8.3) at 3 mo and 6.6 (5.4–7.9). The 3 and 12 mo decreases (2 points) met the study's noninferiority hypothesis ($P = .0026$). IIEF-5 (SHIM) scores were unchanged from baseline (15.1) to 12-mo fu (16.3). EjD: 19% of sexually active. 81% maintained Antegrade Ej. Prostates	At 3 mo: The CD grade 1 persistent events consisted of Ej dysfunction (11%), incontinence (6%), and ED (0%)

Table 1 (continued)

Modality	Study	Study period	Cohort	Median/ mean fu time	Sexual results	Adverse events
					< 100 vs > 100 3 mo: Ej dysfunction, as adjudicated by the CEC, was similar in both groups; 17% of the < 100 cc pts. compared to 14% of the > 100 cc pts. ($P = 1.0$).	
	No. 126130001677763	11/2017–07/2014	21	12 mo	Pts sex active at baseline and at fu: No dec IIEF-15 scores on questions 9 and 10 (Ej dys). In the 11pts sex active, intercourse satisfaction (IIEF-15 questions 6 to 8) increased < 0.01	
	HREC 12/CEN/63: New Zealand Study	01/2013–02/2014	15	6 mo		No retrograde Ej, or ED reported in any patient.
Prostate Artery Embolization	NCT02054013	2/2014–5/2017	99: 48 PAE, 51 TURP	12 wks	IIEF score no sig. Difference PAE vs TURP: PAE: Baseline 15.1 > 14.64 12 wks. TURP: 13.1 > 11.67	
	Embospheres trial: Portugal	7/2015–12/2016	136: 100–300 um (44 pts), B 300–500 um (46 pts), or C 100–500 um (48 pts)	18 mo	Change from baseline IIEF: Group A: Mean: 16.7 (SD6.62), change from baseline: − 4.78 (95% CI: − 16.5 to 6.93) $P = .72$. Group B: Mean: 17.6 (SD 7.82) change from baseline − 5.58 (− 18.0 to 6.870). Group C: Mean 16.9 (SD 8.33), Change from baseline: 8.13% (CI: − 11.9 to 28.2)	Hemsp: 8/137, Group A: 4/43, Group B: 1/46, Group C: 3/48
	Polyvinyl Alcohol (PVA) Particle comparison trial	01/2010–10/2015	120: 60: 50-μm Plus 100-μm; 60: 100-μm	34 mo	IIEF-5 (50 um + 100 um) vs (100 um): Pre-PAE: 15.0 ± 7.5 (4–23) 48 vs. 16.0 ± 7.0 (5–22) 47 $P = 0.784$; 1 mo: 16.0 ± 6.5 (5–21) 55 vs 15.5 ± 7.5 (6–22) 55 $P = 0.892$; 3 mo: 15.5 ± 8.0 (7–23) 54 vs 17.0 ± 9.0 (8–22) 53 $P = 0.070$; 6 mo: 14.5 ± 8.5 (6–25) 54 vs 16.5 ± 7.5 (6–23) 50 $P = .344$; 12 mo: 16.5 ± 7.0 (6–24) 53 vs 16.0 ± 8.5 (6–26) 50 $P = 0.710$; 24 mo: 15.5 ± 6.5 (5–25) 51 vs 16.5 ± 8.5 (6–23) 46 $P = 0.147$. All not sig.	No radiation-related adverse events, ED, or retrograde Ej were observed. Transient Hemsp: Group A 7.3%, Group B: 10.9% $P = 0.778$
	FDA-Approved Investigational Device Exemption Study	12/2014–06/2017	45	12 mo	There were no changes in MSHQ-EjD or IIEF throughout the study duration: insig	1 case hemsp
	CAAE# 36089814.0.0000.0-068 Brazil Study	06/2008–08/2014	97: 59 oPAE, 38 PErFecTED technique	12 mo		Decreased Ejaculate Vol: oPAE 17% vs 10.5% PErFecTED $P = > 0.2$ Transient hemsp: 5.1% vs. 5.3% > 0.2
	PErFecTED vs original PAE vs TURP	11/2010–04/2014	45: 15 oPAE, 15 PErFecTED, 15 TURP	12 mo	IIEF: oPAE: 14.3 ± 6.8 (0–21) ➔ 12.6 ± 7.7 (0–21). Not sig. TURP: 12.5 ± 6.6 (0–21) ➔ 16.1 + − 5.7 (5–21). Stat Sig PErFecTED: 17.3 ± 5.3 (0–22) ➔ 18.7 ± 3.2 (14–24) Not sig	PAE and PErFecTED: hemsp (1/15, 6.7% in both), and reduction in ejaculate vol (2/ 15, 13.3% in oPAE group, 1/15, 6.7% in PErFecTED. Retrograde Ej occurred in all (100%) TURP pts
	NCT02167919	11/2014–10/2015	12	1 mo	IIEF score before 13 ± 8.3 (2.4) after 17 ± 7.2 (2.1) $P < 0.01$. 3 mo fu 15 ± 7.3 (2.1) p 0.19 (2 pt. data limited)	1 transient hemsp. No patient reported ED or retrograde Ej as a result of PAE.

Table 1 (continued)

Modality	Study	Study period	Cohort	Median/ mean fu time	Sexual results	Adverse events
	>80 g Chinese study	2/2009–7/2013	105	24 mo	IIEF no sig changes from baseline	There were no incidences of Ej disorders post-procedure. 1 wk. fu: 8.1% hemsp
	>90 g prostate Brazil	NA	33	3 mo		5.9% hemsp, No Ej disorders post operatively
	United States Isaacson et al.: Prospective	1/2012–3/2013	18	3 mo	At one mo: EF, as measured by IIEF, improved on average from 12.9 to 10.9 ($P = 0.02$). Sexual function improved, although not sig, by 34% at 1 mo ($P = 0.11$), 5% at 3 mo ($P = 0.72$), and 16% at 6 mo ($P = 0.19$).	Three of the 19 pts. (16%) experienced self-limited (ie, < 4 wk) hemsp,
	Urinary Retention Pts: Prospective	06/2008–11/2011	11	28.6 mo	ED measured by IIEF was mild/moderate at 1-mo fu and thereafter improved to mild to no dysfunction ($P = 0.53$)	No ED observed

Ej ejaculation/ejaculatory, *ED* erectile dysfunction, *EF* erectile function, *mo* months, *yrs* years, *Sig* sig/ly, *hemsp* hematospermia

membranes. The water vapor allows for this disruption without any significant rise in temperature within the treatment zone and thereby allowing for no thermal effects outside the targeted treatment zone [18••]. Rezūm received an FDA approval as a treatment alternative to TURP for BPH in 2015 [43].

Two major clinical trials have investigated the efficacy and sexual results of Rezūm. McVary et al. performed a prospective clinical trial investigating patients for a change in MSHQ-EjD scores. Changes from the baseline were insignificant at 12-month and 24-month intervals. However, MSHQ declined significantly 14.2% and 18.0% at 36 and 48 months, respectively, after surgery. There was also an insignificant change in the IIEF-EF scores from the baseline for the first 3 years. However, there was a significant decline in the score at 48-month follow-up ($P = 0.0333$). The MSHQ bother score (12 months $P = 0.0017$, 24 months $P = 0.0118$, 36 months $P = 0.0153$) had a significant decline for all endpoints except the 48-month follow-up. No adverse events related to ejaculation were reported. Dixon et al. reported similar changes from the baseline. The IIEF scores significantly increased at 3-month, 6-month, and 12-month follow-ups ($P = 0.041$ for 12 months). No sexually related adverse events were reported.

Prostatic Urethral Lift

The prostatic urethral lift (PUL) is a minimally invasive surgery which involves the retraction of the obstructing prostatic lobes through the use of mechanical implants inserted through the urethra. These implants then hold the lobes out of place, thereby opening the prostatic urethra [44]. The aim of the procedure is to create an anterolateral channel encompassing the bladder neck to the verumontanum [45]. Under the trade name UroLift®, PUL was approved for the treatment of BPH by the FDA in 2013 [46]. UroLift® is not for every patient with BPH, including those with prostates larger than 100 g or those with large obstructing median lobes [47].

Two randomized clinical trials have been performed to evaluate the efficacy and sexual effects of PUL. The L.I.F.T trial was a comparative trial against a sham procedure investigating the long-term outcomes of UroLift®. Changes in the MSHQ-EjD compared with the baseline were significant for all follow-up periods. ($P < 0.0001$). At 3 months, there was an increase of the MSHQ score of 36%; at 12 months, 28%; at 2 years, 30%; at 3 years, 9%; and at 4 years, 12%. There was a positive change in the SHIM at all time periods as well. At 3 months, + 1.3 compared with the baseline; at 12 months, + 0.7; at 2 years, + 1.1; at 3 years, + 0.5; and at 4 years, + 0.3. The MSHQ-EjD bother score compared with the baseline was also significant for all follow-up times ($P < 0.0001$). IIEF changes were insignificant from the baseline after the 24-month follow-up. The second trial was a comparative trial against TURP. Changes from the baseline

were significant for the UroLift® group in the MSHQ-EjD and were significantly different when compared with TURP for all follow-up periods (at 2 years $P < 0.001$). At the maximal follow-up point of 2 years for PUL group, the MSHQ-EjD increased by 2.8%. In TURP group, the same score decreased by 55.1%. Although there were changes in MSHQ-EjD bother and IIEF scores from the baseline, these changes were not significantly different from the TURP changes from the baseline. In either trial, there was no incidence of sexually adverse events including sustained ED or RE.

Prostate Artery Embolization

Prostatic or prostate artery embolization (PAE) is an FDA-approved treatment for BPH. PAE involves the cannulation and the embolization of the prostatic arteries leading to the ischemic shrinking of the prostate gland [48]. Patients undergoing the procedure must first receive MRI imaging as well as a contrast CT to verify the patency of the prostatic arteries [49]. Access to the prostatic arteries is generally through the groins or the arms. PAE is generally performed by interventional radiologists, and the current AUA guidelines state that PAE is not recommended for the treatment of LUTS attributed to BPH outside of the context of a clinical trial (Guideline Statement 22).

Multiple clinical trials have been performed to investigate the efficacy and sexual function results of PAE. Two trials compared PAE with TURP in terms of the IIEF scores. A trial investigating 99 patients, 48 undergoing PAE and 51 undergoing TURP, found an insignificant difference in IIEF changes from the baseline for PAE when compared with TURP after 12 weeks (a change of 15.1 to 14.64 and a change of 13.1 to 11.67 for PAE and TURP, respectively) [29]. TURP was again compared to PAE in a trial investigating 12-month outcomes of PAE, TURP, and PerFecTED. PerFecTED is PAE in which the proximal embolization is performed first and then followed by embolization distally [50]. In this trial, the IIEF score change from the baseline was insignificant for both PAE and PerFecTED but significant for TURP. However, although 100% of patients in the TURP group developed RE, no patients in either PAE group developed RE [32]. In none of the trials investigating IIEF were changes in score significantly changed over time. No trials reported RE or other EjD besides one trial which reported a decreased ejaculate volume in 13.3% of patients who received oPAE and 6.7% of patients who received PerFecTED. The most common sexual side effect was transient hematospermia post-operatively.

Aquablation

Aquablation is a novel minimally invasive water ablation therapy utilizing imaging and robotics to ablate and remove prostatic tissue (AquaBeam®, Procept BioRobotics, Redwood Shores, CA, USA). Aquablation utilizes high-pressure and high-velocity saline for the target removal of the prostatic tissue using image guidance. The procedure involves the urologist inserting the ablation probe through the urethra. The surgeon then maps out the area to be ablated on an image-guided screen. The robotic probe then ablates the mapped area of the prostate using the high-pressured saline [25]. According to the AUA, Aquablation may be offered to patients with LUTS from BPH with prostates between 30 and 80 g (Conditional Recommendation; Evidence level: Grade C).

Four clinical trials were in included in this systematic review. The two major trials investigating Aquablation are WATER and WATER II. WATER (Waterjet Ablation Therapy for Endoscopic Resection of Prostate Tissue) is a prospective double-blind multicenter trial comparing TURP and Aquablation. In investigating 184 patients, 117 Aquablation and 67 TURP, a 6-month follow-up revealed a lower anejaculation rate for those treated with Aquablation when compared with TURP (10% vs 36%, $P = 0.0003$). The decrease in MSHQ-EjD and IIEF-5 scores was higher in TURP compared with Aquablation (33% versus 56%, $P = 0.0268$). In sexually active men, the mean EF scores on IIEF-15 were stable after Aquablation, but decreased after TURP. The overall sexual satisfaction after Aquablation was significantly better ($P = 0.0492$). Ejaculatory function scores on MSHQ-EjD were stable after Aquablation but significantly worse after TURP ($P = 0.0254$) At 6 months, the overall sexual dysfunction as an adverse event was 0 for Aquablation and 1 (1.5%) for TURP ($P = 0.3591$). WATER II was a subsequent trial which investigated men with prostates between 80 and 150 g. One hundred-one patients were followed for 12 months. The MSHQ-EjD decreased from the baseline by 2 points ($P = 0.0026$). The IIEF-5 (SHIM) scores were unchanged from the baseline (15.1) to the 12-month follow-up (16.3). Ejaculatory dysfunction was present in 19% of sexually active men, while 81% maintained antegrade ejaculation. At the 3-month follow-up, 11% reported ejaculatory dysfunction as an adverse event, and none reported ED. Two other trials with smaller cohort sizes also investigated Aquablation [23]. Neither trials had patients reporting the side effect of RE or ED. In 11 patients who were sexually active, there was an increase in intercourse satisfaction (IIEF-15 questions 6 to 8) $P < 0.01$.

Discussion

Novel minimally invasive therapies for the treatment of BPH have multiplied in recent years. Newer therapies have mainly focused on reducing post-operative recovery and adverse events. One of the most established side effects of the traditional TURP is ejaculatory dysfunction. This includes RE which may pose a larger problem with men being diagnosed

and treated for BPH at a younger age [51]. With the advent of these minimally invasive treatment modalities, sexual dysfunction post-operatively has been investigated. All four treatment modalities, Rezūm, UroLift®, PAE, and Aquablation, demonstrate lower ejaculatory dysfunction than TURP; however, Rezūm has not undergone a matched trial with TURP. In one study on Rezūm, 4.4% EjD was reported; however, most studies reported 0% EjD. For both clinical trials focused on prostatic urethral lift, 0% EjD was reported. For PAE, one trial reported 13.3% loss of ejaculatory volume, while most PAE studies did not report EjD values. For Aquablation, 19% EjD was reported in one trial.

As these treatment modalities all aim to preserve ejaculatory dysfunction, determining which modality is suitable for a particular patient may be based on surgeon preference and inclusion criteria for each. Water vapor thermal therapy and PUL are the only therapies under the 2019 AUA guidelines which may be offered to patients who desire the preservation of erectile and ejaculatory functions (Conditional Recommendation; Evidence Level: Grade C). Aquablation trials revealed some level of EjD following the procedure, and PAE is still controversial among urologists as it is mainly performed by interventional radiologists.

The included trials were not without limitations. First, many of the trials with long-term outcomes (greater than 12 months) had attrition and, therefore, only included results from patients who remained in the follow-up. Many of the questionnaires are subjective and based on patient answers. These survey results may differ based on location and cultural influences. One study was eliminated just before analysis from review due to no reporting on sexually adverse events reflecting cultural norms [22]. Furthermore, BPH is generally a disease of the elderly which may have influenced ejaculation-related results, as many men of this age group may already suffer from erectile dysfunction. This may have caused sexually related adverse events to be under reported. In a few studies, ejaculation was originally not investigated and was only explored as a function of sexual questionnaires (such as IIEF or SHIM). The amount of trials on each modality differed greatly. PAE was the most heavily studied of the four trials due to a longer history of use. In the newest study, Aquablation still does not have long-term follow-up beyond the first 12 months. This may have affected the results as long-term follow-up is available for the other three modalities. Finally, this review was not without limitations, as some results or trials which were not available on the chosen online database may have been overlooked. Additionally, this review only focuses on the sexual results of these interventions, and thus, the efficacy of the included modalities may differ. We expect that further prospective studies in which participants are match by comorbidities and prostate size will provide further insights into the ejaculation and the sexual outcomes of the minimally invasive treatment modalities for BPH.

No head-to-head study has compared the four selected treatment modalities to each other. With the growing number of minimally invasive treatments offered to patients for BPH-related LUTS, it is imperative to have direct efficacy and safety comparisons of these treatments. Further research should also focus on developing techniques to decrease sexual side effects.

Conclusions

The systematic review of novel modalities for BPH-related LUTS revealed improved post-operative ejaculation metrics compared to traditional treatment. The water vapor thermal therapy of Rezūm, PUL or UroLift®, PAE, and Aquablation showed acceptable rates of RE and had very low adverse events related to the procedure. Ultimately, all four treatment modalities are comparable in terms of sexual side effects, with clinical trials of Rezūm, PUL, and PAE showing minimal to no RE events post-operatively. PUL and Rezum both demonstrated lower rates of ejaculatory dysfunction while preserving MSHQ-EjD scores when compared to PAE and Aquablation. Further research is required to directly compare these treatment modalities in a randomized clinical trial.

Code Availability None used

Data Availability This is a literature review, all data is available through online peer reviewed articles.

Compliance with Ethical Standards

Conflict of Interest No conflicts of interest or disclosures

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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