Prostatic Diseases and Male Voiding Dysfunction

Which Anatomic Structures Should Be Preserved During Aquablation Contour Planning to Optimize Ejaculatory Function? A Case-control Study Using Ultrasound Video Recordings to Identify Surgical Predictors of Postoperative Anejaculation

David-Dan Nguyen, Surag S. Mantri, Kevin C. Zorn, Vincent Misraï, Dean Elterman, and Naeem Bhojani

OBJECTIVE To identify key anatomic structures that should be preserved to decrease postoperative anejaculation after Aquablation.

METHODS We conducted a case-control study design using patient data and operative video logs from Aquablation clinical trials. Cases were sexually active participants with functional baseline ejaculation and postoperative anejaculation. Controls were sexually active participants with functional baseline ejaculation and no postoperative decline in sexual function. Each case was matched to 1 or 2 controls. Video logs from the procedure were scored for: verumontanum cut coverage, penetration of ejaculatory ducts, depth of cut below the verumontanum, angle offset of verumontanum to centerline of protection zone, number of passes, and intraprostatic calcifications. Conditional logistic regression was used to calculate univariate odds ratios relating anatomic findings to case/control status.

RESULTS We identified 24 cases and 27 controls. In univariate analysis, predictors of postoperative anejaculation were: penetration of the ejaculatory ducts (odds ratio [OR] 8.6 [95% CI 1.09-67.5], $P = .041$) and depth below the verumontanum (OR 1.92 [1.1-3.3], $P = .015$).

CONCLUSION Violation of anatomic structures involved in ejaculation during the Aquablation procedure increases the risk of postoperative anejaculation. More careful attention to these structures during contour planning may further improve ejaculatory function after Aquablation. UROLOGY 00: 1–6, 2021. © 2021 Elsevier Inc.

The maintenance of sexual function can be of great concern for patients undergoing surgery to treat lower urinary tract symptoms (LUTS) due to benign prostatic obstruction (BPO) as a result of benign prostatic hyperplasia (BPH).[1,2] Preserving ejaculation in these men is thus important as it is a fundamental domain of male sexual function.[3] However, loss of antegrade ejaculation and anejaculation after BPO surgery are common.[4,5] Ejaculatory dysfunction (EjD) is almost inevitable with conventional transurethral resection of the prostate (TURP) and affects a majority of patients undergoing photoselective vaporization of the prostate (PVP), holmium laser enucleation of the prostate, and open simple prostatectomy.[5-11] Novel ablative therapies, such as Aquablation, have shown promise in reducing EjD after surgery.[12,13] Aquablation is a semi-autonomous, robotically executed, surgeon-guided, high-pressure, heat-free water jet technology leveraging real-time, intraoperative ultrasound

From the Faculty of Medicine, McGill University, Montreal, QC, Canada; the PROCEPT BioRobotics, Redwood City, CA, USA; the Division of Urology, Centre hospitalier de l'Université de Montréal (CHUM), Université de Montréal, Montreal, QC, Canada; the Department of Urology, Clinique Pasteur, Toulouse, France; and the Division of Urology, University Health Network (UHN), University of Toronto, Toronto, ON, Canada

Address correspondence to: Naeem Bhojani, M.D., University of Montreal Hospital Center, 900 St. Denis, R08.474, Montréal, Québec, H2X 0A9.

E-mail: naeem.bhojani@gmail.com

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visualization of the prostate.[14] A higher proportion of patients undergoing Aquablation compared to TURP maintain antegrade ejaculation in both small 30cc-to-80cc (89%) and large 80cc-150cc (81%) prostates.[15,16]

The specific reasons why novel therapies are associated with improved maintenance of antegrade ejaculation remains unclear. It is commonly accepted that EjD is rare in therapies and techniques that preserve the neurovascular bundles as ejaculation requires contraction of the external sphincter and bulbar urethra.[17] It is also hypothesized that the resection of the bladder neck results in retrograde ejaculation − however, some patients with opened bladder necks after surgery have been shown to have preserved antegrade ejaculation, while other patients with preserved bladder necks have developed EjD.[18] As such, it has also been hypothesized that there are other anatomic structures that play an important role in maintaining ejaculatory function and that these structures should be preserved during the surgery to maximize sexual outcomes. One leading theory regarding preservation of ejaculatory function describes avoiding damage to the precollicular and para-collicular tissue in the area where the ejaculatory ducts emerge near the verumontanum in the distal apical tissue.[5,17-20]

Previous studies exploring the effect of preserving certain anatomic structures on postoperative sexual outcomes are limited by their ability to reliably describe and measure intraoperative events that may impact ejaculatory function. Considering that all Aquablation procedures require ultrasound visualization of the prostate and are robotically executed, it is possible to consistently assess which anatomic structures were resected and to what extent by reviewing the intraoperative ultrasound video logs. As such, leveraging this unique feature of Aquablation, we sought to determine the intraoperative anatomic predictors of EjD after Aquablation.

METHODS

Study Design and Data Source

We conducted a case-control study using patient data and operative video logs from the WATER (NCT02505919), WATER II (NCT03123250), and WATER FRANÇAIS (NCT03191734) Aquablation clinical trials.[21-23]

WATER (Waterjet Ablation Therapy for Endoscopic Resection of Prostate Tissue) is a prospective, double-blind, multicenter, international clinical trial of Aquablation compared to TURP for the treatment of LUTS due to BPO in men with a prostate volume between 30cc and 80cc. Promising results in larger prostates motivated investigator to then conduct WATER II, a prospective, multicenter, international clinical trial of Aquablation for the surgical treatment of LUTS due to BPO in men with a prostate volume between 80cc and 150cc. FRANÇAIS WATER is a prospective, single-arm clinical trial of Aquablation for the surgical treatment of LUTS due to BPO in men with prostate volumes between 30cc and 80cc. The trial was conducted at 3 centres in France.

Intervention and Contour Planning

All patients underwent Aquablation. Aquablation is a robotically executed resective surgical treatment for LUTS related to BPH. The description of the technology and technique can be found in the study presenting the initial clinical experience with Aquablation.[14] Of particular relevance to our study, Aquablation relies on live, intraoperative imaging of the prostate using a bi−plane transrectal ultrasound (TRUS) probe. During the contour planning phase of the procedure, using measurements from the TRUS image, the dimensions are inputted into the console and the surgeon maps the area of the prostate tissue to be resected. Once contour planning is completed, the surgeon initiates the automated, robotically executed procedure.

Matching

Cases were sexually active participants who had functional ejaculation at baseline based on preoperative Male Sexual Health Questionnaire-EjD (MSHQ-EjD) scores of 8 or greater and who reported a postoperative score of zero for question 3 of the MSHQ-EjD (How would you rate the amount or volume of semen or fluid when you ejaculate? A score of "0" equates to an answer of "could not ejaculate"). Controls were similar sexually active participants who had baseline functional ejaculation but their postoperative MSHQ-EjD scores did not decrease substantially and they did not answer "0" for question 3 of the MSHQ-EjD. Each case was manually matched to 1 or 2 controls from the same study with similar prostate sizes by transrectal ultrasound (±10 cc) and similar baseline MSHQ-EjD scores.

Recording Review and Anatomic Predictors of Interests

Procedural video logs from the AquaBeam Robotic System's central processing unit were retrospectively reviewed and scored by an expert blinded to all patient outcomes, including anejaculation. As such, the expert reviewer was blinded to the case/control status of the video log. The expert (SM) led the development of the AquaBeam Robotic System and had previously reviewed more than 1,000 Aquablation cases.

The critical parameters and anatomic structures evaluated were selected following a review of the literature and consultation with BPH surgery experts. The selected intraoperative parameters included: verumontanum cut coverage as a percent of the distance from the external sphincter to verumontanum in the sagittal plane where complete coverage of the verumontanum was deemed 100% (Fig. 1A), whether ejaculatory ducts were penetrated via illumination on the ultrasound image due to the hyperechoic artifact by penetration of the turbulent water, approximate posterior depth of contour plan below the peak verumontanum on sagittal images (Fig. 1B), approximate angle offset of verumontanum to centerline of protection zone, number of passes, and intraprostatic calcifications. The linear measurements were calibrated based on the ultrasound X-Y scale grid.

Statistical Analysis

Conditional logistic regression was used to calculate univariable and multivariable odds ratios relating anatomic findings to case/control status. In multivariable analysis, in addition to the anatomic predictors of interest, we also adjusted for age and body mass index (BMI) as both have been shown to be associated with EjD.[24,25]

All statistical analyses were performed using the R programming language. Statistical significance was defined as a 2-sided $P < .05$.

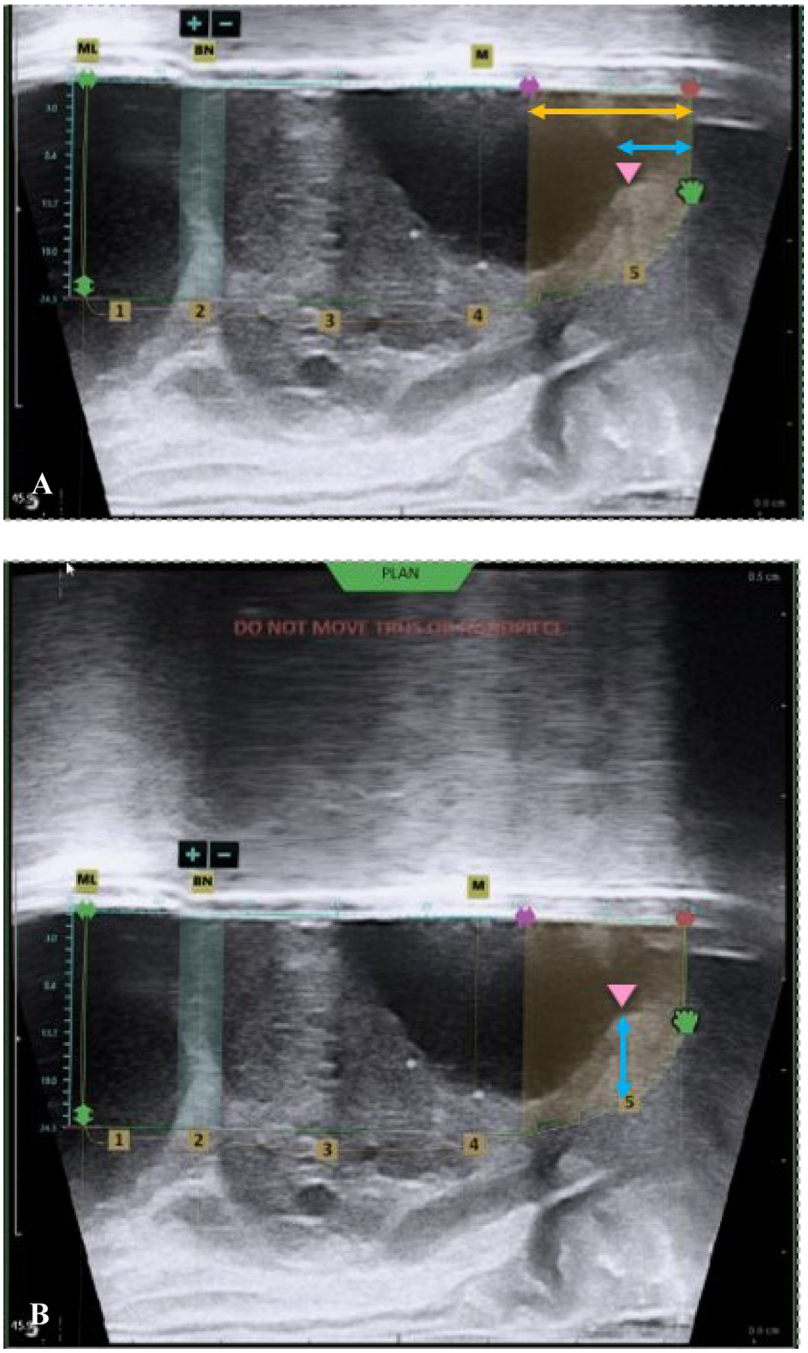

Figure 1. Verumontanum coverage with butterfly cut (A) and posterior depth below the veru peak (B). (Color version available online.)

RESULTS

Baseline demographics

We identified 24 cases which were matched to 27 controls. The 24 cases and 27 controls had preoperative mean prostate volumes of 82 and 81 cc, respectively. Cases had a slightly lower BMI compared to controls (p=0.03). Additional baseline demographics can be found in Table 1.

Predictors of Anejaculation

In univariable analysis, statistically significant predictors of postoperative of EjD were: penetration of the ejaculatory ducts (odds ratio [OR] 8.6 [95% CI 1.09-67.5], P = .041) and depth below the verumontanum (OR 1.92 [1.1-3.3], P = .015). Controlling for age, BMI, or both age and BMI did not affect the resulting effect size of the odds ratios for penetration of the ejaculatory ducts (OR 8.5, 8.1 and 8.1, P =.043, .049 and .05, respectively) and depth below the verumontanum (OR 2.1, 2.0 and 2.1, P = .027, .029 and .043, respectively). Verumontanum cut coverage percent was lower in cases compared controls (OR 0.96 [95% CI 0.91-1.00], P = .051) as did number of passes (OR 0.1 [0.01 - 1.1], P = .056), but these factors did not meet the threshold of significance for predictors of anejaculation.

Table 1. Baseline characteristics of cases and matched controls

	Cases (*n*=24)	Controls (*n*=27)	*P* Value
Prostate volume (cc), mean (SD) [range]	82 (35.6) [31-138]	81.0 (33.7) [30-142]	.9185
Age (years), mean (SD) [range]	65.8 (7.4) [54-80]	64.6 (6.8) [53-79]	.5620
Body mass index (kg/m^2), mean (SD) [range]	26.3 (2.2) [20.4-29.4]	27.9 (2.9) [23.9-33.8]	**.0302**

*Note that prostate volume was used for matching.

In multivariable analysis using the selected 6 measures, no independent predictors were statistically significant, but verumontanum depth was associated with an elevated OR (2.92 [0.90-9.45], P = .073).

DISCUSSION

Preserving sexual function is a prevalent consideration among patients undergoing surgery for LUTS due to BPO — it can also be a priority, especially for younger men.[1,2,5] While novel therapies such as Aquablation have been shown to be associated with fewer sexual side-effects, it is unclear which intraoperative factors are associated with preserved antegrade ejaculation. Furthermore, since Aquablation is done under real-time visualization and because intraoperative ultrasound video logs were available for all clinical trial procedures, we were able to investigate, using a blinded case-control design, the impact of several anatomic factors on the development of postoperative anejaculation. Our findings suggest that the depth of the cut below the verumontanum and penetration of the ejaculatory ducts are predictors of postoperative Aquablation EjD.

Preserving the para-collicular and nearby tissue, which is located 1 cm proximal to the verumontanum, is related to the importance of the musculus ejaculatorius and the verumontanum itself for ejaculation.[17-20] Additionally, the Aquablation butterfly cut, which is a modified ablation of the apical tissue that preserves the area around the verumontanum, follows the same principles as previous ejaculatory sparing techniques preserving the para-collicular prostate tissue/ejaculatory hood reported in the literature with different modallities.[5,26-30] For example, Talab et al reported a modified PVP technique that preserved the bladder neck muscle fibers as well as the pre-collicular tissue and para-collicular tissue of the prostate. They found significantly lower rates of anejaculation, with fewer than 15% of their cohort developing anejaculation and over half reporting no change in their postoperative ejaculation function.[28] Similarly to what we report with Aquablation and what Talab et al described with PVP, Alloussi et al reported outcomes of a modified technique for TURP emphasizing the preservation of the ejaculatory hood and found that 79 out of 87 patients preserved antegrade ejaculation at 3 months after surgery.[27] As such, our findings further support the hypothesis that not resecting or damaging the tissue posterior to the verumontanum results in the most significant maintenance of antegrade ejaculation without impairing Qmax.[5,30] However, compared to these ejaculation-sparing techniques, it is more likely that our findings are externally generalizable considering the image guidance and robotic execution provided by the Aquablation system.[31] Indeed, while these modified approaches are likely associated with a certain learning curve, modifications to the Aquablation procedure simply require greater attention to key structures during the contour planning phase.

By preserving key anatomic structures, it is thus possible to further reduce rates of anejaculation after Aquablation, which are already low. In the WATER (30-80mL), WATER II (80-150mL), and WATER FRANÇAIS trials, antegrade ejaculation was maintained in 89%, 81%, and 73% of patients, respectively.[15,23] It is important to note that Aquablation is the only procedure where de novo EjD remained low despite larger prostate sizes (80cc-150cc).[12,15,16] Other surgical modalities available for prostates sizes >80cc, such as PVP, holmium laser enucleation of the prostate , and OSP are associated with postoperative EjD in 60%-80% of cases.[5,10,32] It is possible that the anatomic precision of Aquablation prostate resection helps to avoid damage to structures that are key to preserve ejaculation, such as the verumontanum.

Our study is not without limitations. First, the Aquablation ultrasound recordings were reviewed by a human expert which may introduce human error or cognitive bias. However, the expert was blinded to case/control status and there is no reason to believe that human error and related biases differentially affected measurements between cases and controls. Additionally, our review of intraoperative recordings is particularly reliable due to 2 of Aquablation's features — a precise robotic execution of the surgery guided by surgeon-planning and high-quality ultrasound imaging. These features allow precise determination of the location of structures and the resecting waterjet. A second limitation is that it was not possible to further characterize the EjD of the cases. For example, we did not ascertain if the cases had retrograde ejaculation. Third, we did not account for a number of factors that have been shown to be predictors of postoperative sexual outcomes, such as underlying comorbidities. Finally, despite a large number of trial participants, our sample size was relatively limited due to the small number of participants who had postoperative EjD. Analysis of a larger dataset and commercial experience may help to determine the role of other anatomic factors in predicting anejaculation after Aquablation. Additionally, double-blind, randomized controlled trials of different Aquablation approaches would further confirm our suggested findings.

CONCLUSION

In conclusion, damage to anatomic structures involved in ejaculation during the Aquablation procedure, specifically

planning too far posteriorly below the verumontanum or penetrating the ejaculatory ducts, is associated with greater odds of postoperative anejaculation. More careful attention to anatomic structures during the contour planning phase may further reduce postoperative EjD after Aquablation. Our findings contribute to the growing body of evidence suggesting that preservation of the tissue surrounding the verumontanum plays an important role in postoperative ejaculatory function, regardless of the surgical modality.

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References

1. Bouhadana D, Nguyen DD, Zorn KC, Elterman DS, Bhojani N. Patient perspectives on benign prostatic hyperplasia surgery: a focus on sexual health. *J Sex Med*. 2020. https://doi.org/10.1016/j.jsxm.2020.07.006.
2. Laumann EO, Paik A, Glasser DB, et al. A cross-national study of subjective sexual well-being among older women and men: findings from the global study of sexual attitudes and behaviors. *Arch Sex Behav*. 2006;35:145–161. https://doi.org/10.1007/s10508-005-9005-3.
3. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology*. 1997;49:822–830. https://doi.org/10.1016/S0090-4295(97)00238-0.
4. Cornu JN, Herrmann T, Traxer O, Matlaga B. Prevention and management following complications from endourology procedures. *Eur Urol Focus*. 2016;2:49–59. https://doi.org/10.1016/j.euf.2016.03.014.
5. Leong JY, Patel AS, Ramasamy R. Minimizing sexual dysfunction in BPH surgery. *Curr Sex Heal Reports*. 2019;11:190–200. https://doi.org/10.1007/s11930-019-00210-1.
6. Donovan JL, Peters TJ, Neal DE, et al. A randomized trial comparing transurethral resection of the prostate, laser therapy and conservative treatment of men with symptoms associated with benign prostatic enlargement: the CLasP study. *J Urol*. 2000;164:65–70. https://doi.org/10.1016/S0022-5347(05)67450-2.
7. Marra G, Sturch P, Oderda M, Tabatabaei S, Muir G, Gontero P. Systematic review of lower urinary tract symptoms/benign prostatic hyperplasia surgical treatments on men's ejaculatory function: time for a bespoke approach? *Int J Urol*. 2016;23:22–35. https://doi.org/10.1111/iju.12866.
8. Thomas JA, Tubaro A, Barber N, et al. A multicenter randomized noninferiority trial comparing greenlight-xps laser vaporization of the prostate and transurethral resection of the prostate for the treatment of benign prostatic obstruction: two-yr outcomes of the GOLIATH study. *Eur Urol*. 2016;69:94–102.
9. Ahyai SA, Lehrich K, Kuntz RM. Holmium Laser Enucleation versus Transurethral Resection of the Prostate: 3-Year Follow-Up Results of a Randomized Clinical Trial. *Eur Urol*. 2007;52:1456–1464. https://doi.org/10.1016/j.eururo.2007.04.053.
10. Bachmann A, Tubaro A, Barber N, et al. 180-W XPS GreenLight Laser Vaporisation Versus Transurethral Resection of the Prostate for the Treatment of Benign Prostatic Obstruction: 6-Month Safety and Efficacy Results of a European Multicentre Randomised Trial—The GOLIATH Study. *Eur Urol*. 2014;65:931–942. https://doi.org/10.1016/J.EURURO.2013.10.040.
11. Jones P, Alzweri L, Rai BP, Somani BK, Bates C, Aboumarzouk OM. Holmium laser enucleation versus simple prostatectomy for treating large prostates: Results of a systematic review and meta-analysis. *Arab J Urol*. 2016;14:50–58. https://doi.org/10.1016/j.aju.2015.10.001.
12. Bhojani N, Bidair M, Zorn KC, et al. Aquablation for Benign Prostatic Hyperplasia in Large Prostates (80-150 cc): 1-Year Results. *Urology*. 2019;129:1–7. https://doi.org/10.1016/j.urology.2019.04.029.
13. Lebdai S, Chevrot A, Doizi S, et al. Do patients have to choose between ejaculation and miction? A systematic review about ejaculation preservation technics for benign prostatic obstruction surgical treatment. *World J Urol*. 2018;37:1–10. https://doi.org/10.1007/s00345-018-2368-6.
14. Gilling P, Reuther R, Kahokehr A, Fraundorfer M. Aquablation - image-guided robot-assisted waterjet ablation of the prostate: initial clinical experience. *BJU Int*. 2016;117:923–929. https://doi.org/10.1111/bju.13358.
15. Nguyen DD, Barber N, Bidair M, et al. Waterjet Ablation Therapy for Endoscopic Resection of prostate tissue trial (WATER) vs WATER II: comparing Aquablation therapy for benign prostatic hyperplasia in 30−80 and 80−150 mL prostates. *BJU Int*. 2020;125:112–122. https://doi.org/10.1111/bju.14917.
16. Bhojani N, Nguyen DD, Kaufman RP, Elterman D, Zorn KC. Comparison of< 100 cc prostates and>100 cc prostates undergoing aquablation for benign prostatic hyperplasia. *World J Urol*. 2019;37:1361–1368. https://doi.org/10.1007/s00345-018-2535-9.
17. Gil-Vernet JM, Alvarez-Vijande R, Gil-Vernet A, Gil-Vernet JM. Ejaculation in men: a dynamic endorectal ultrasonographical study. *Br J Urol*. 1994;73:442–448. https://doi.org/10.1111/j.1464-410X.1994.tb07612.x.
18. Lang C, Eichel R, Alloussi SH, Alloussi S. V12 Ejaculation Preserving (EP) technique in endourological treatment of bpheplaservaporesection and eptur of the prostate. *Eur Urol Suppl*. 2009;8:385. https://doi.org/10.1016/S1569-9056(09)61029-0.
19. Hermabessiere J, Guy L, Boiteux JP. [Human ejaculation: physiology, surgical conservation of ejaculation]. 1999;9:305-309.
20. Sturch P, Woo HH, McNicholas T, Muir G. Ejaculatory dysfunction after treatment for lower urinary tract symptoms: retrograde ejaculation or retrograde thinking? *BJU Int*. 2015;115:186–187. https://doi.org/10.1111/bju.12868.
21. Gilling P, Barber N, Bidair M, et al. WATER: a double-blind, randomized, controlled trial of aquablation vs transurethral resection of the prostate in benign prostatic hyperplasia. *J Urol*. 2018;199:1252–1261. https://doi.org/10.1016/j.juro.2017.12.065.
22. Desai M, Bidair M, Zorn KC, et al. Aquablation for BPH in large prostates (80-150cc): 6-month results from the WATER II Trial. *BJU Int*. 2019. https://doi.org/10.1111/bju.14703.
23. Misrai V, Rijo E, Zorn KC, Barry-Delongchamps N, Descazeaud A. Waterjet ablation therapy for treating benign prostatic obstruction in patients with small- to medium-size glands: 12-month results of the first french aquablation clinical registry. *Eur Urol*. 2019;76:667–675.
24. Vallancien G, Emberton M, Harving N, Van Moorselaar RJA. Sexual dysfunction in 1,274 European men suffering from lower urinary tract symptoms. *J Urol*. 2003;169:2257–2261. https://doi.org/10.1097/01.ju.0000067940.76090.73.
25. Andersen I, Heitman BL, Wagner G. Obesity and sexual dysfunction in younger danish men. *J Sex Med*. 2008;5:2053–2060. https://doi.org/10.1111/j.1743-6109.2008.00920.x.
26. Abdel-Basir Sayed M. Bladder neck resection with preservation of antegrade ejaculation: basir technique. *J Endourol*. 2003;17:109–111. https://doi.org/10.1089/08927790360587441.
27. Alloussi SSH, Lang C, Eichel R, Alloussi SSH. Ejaculation-preserving transurethral resection of prostate and bladder neck: short- and long-term results of a new innovative resection technique. *J Endourol*. 2014;28:84–89. https://doi.org/10.1089/end.2013.0093.
28. Talab SS, Santiago-Lastra YA, Bachmann A, et al. V403 the impact of ejaculation-preserving photo-selective vaporization of the prostate (EP-PVP) on lower urinary tract symptoms and ejaculatory function: results of a multicenter study. *J Urol*. 2013;189. e164-e164.
29. Kim M, Song SH, Ku JH, Kim H-JJ, Paick J-SS. Pilot study of the clinical efficacy of ejaculatory hood sparing technique for

ejaculation preservation in Holmium laser enucleation of the prostate. *Int J Impot Res*. 2015;27:20–24. https://doi.org/10.1038/ijir.2014.22.

30. Chung A, Woo HH. Preservation of sexual function when relieving benign prostatic obstruction surgically: can a trade-off be considered? *Curr Opin Urol*. 2016;26:42–48. https://doi.org/10.1097/MOU.0000000000000247.
31. Nguyen D-D, Bhojani N, Zorn KC. Furthering the external validity of Aquablation and implications for real-world patients. *World J Urol*. 2019:1–2. https://doi.org/10.1007/s00345-018-2610-2.
32. Kuntz RM, Lehrich K, Ahyai SA. Holmium laser enucleation of the prostate versus open prostatectomy for prostates greater than 100 grams: 5-year follow-up results of a randomised clinical trial. *Eur Urol*. 2008;53:160–168. https://doi.org/10.1016/J.EURURO.2007.08.036.