Urodynamic Outcomes After Aquablation

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OBJECTIVES To compare urodynamic outcomes between Aquablation vs transurethral resection of the prostate (TURP).

METHODS Patients were randomized 2:1 (Aquablation:TURP) in the Waterjet Ablation Therapy for Endoscopic Resection of prostate tissue study. Urodynamics were measured at baseline and 6 months.

RESULTS Urodynamics studies were performed in 66 of the participating subjects at baseline and 6 month follow-up. At mean baseline pDet@qmax was 71 and 73 cm H20 in the Aquablation and TURP groups, respectively ($P = .7031$). At 6-month follow-up, pDet@qmax decreased by 35 and 34 cm H20, respectively ($P < .0001$ compared to baseline for both arms) with no significant difference in decrease across groups ($P = .8919$). A large negative shift in Bladder Outlet Obstruction Index was observed, consistent with a large reduction in the proportion of subjects with obstruction at follow-up compared to baseline (79% to 22% in Aquablation and 96% to 22% in TURP).

CONCLUSIONS In this trial, improvements after Aquablation in objective measures of bladder outlet obstruction were similar to those observed after TURP. ClinicalTrials.gov number, NCT02505919 UROLOGY 126: 165−170, 2019. © 2019 Elsevier Inc.

Benign prostatic obstruction (BPO) due to benign prostatic hyperplasia (BPH) can cause lower urinary tract symptoms (LUTS) such as urinary hesitancy, frequency, dysuria and secondary complications such as urinary tract infections, bladder stones, renal impairment and urinary retention, which significantly impact quality of life (QOL).[1] Affecting 30% of men over 50 years old, the incidence of BPH increases dramatically with age.[2,3] In recent years, there has been an increasing interest in minimally invasive surgical therapies as alternatives to the current gold standard, electrocautery-based transurethral resection of the prostate (TURP). One of these alternatives, Aquablation, is currently being studied in a phase III double-blind randomized clinical trial—the Waterjet Ablation Therapy for Endoscopic Resection of prostate tissue (WATER) trial. The AquaBeam system uses a robotically controlled high-velocity saline for prostate ablation via a transurethral approach. Prior to ablation, transrectal ultrasound is used for mapping to limit the ablation zone to the transitional zone of the prostate and to spare the verumontanum, resulting in a highly targeted therapy that potentially avoids harmful effects of thermal energy[4,5] and inadvertent destruction of anatomic structures involved in ejaculation. Initial results show that the clinical efficacy of Aquablation is noninferior to TURP, with fewer complications.[6]

As part of the initial assessment of patients presenting with LUTS, urodynamic studies (UD) can provide objective diagnostic information that may aid in patient selection for invasive treatment.[7,8] Repeated postoperatively, UD provide objective evidence of improvement in bladder function and may help predict patient benefit including long-term outcomes.[7] This paper compares short-term urodynamic outcomes after Aquablation and TURP from the WATER Aquablation trial.

METHODS

WATER is a prospective, double-blind multicenter randomized clinical trial assessing the safety and efficacy of Aquablation vs TURP in the treatment of BPH.[6] Participants in the WATER trial included men aged 45-80 years old with prostate sizes from 30-80 grams, International Prostate Symptom Scores (IPSS) ≥ 12, and a maximum urinary flow rate (Qmax) <15 mL/s. Exclusions were: a history of prostate or bladder cancer, neurogenic bladder, bladder calculus, significant bladder diverticulum, active urinary tract infection, treatment for chronic prostatitis, diagnosed urethral stricture, meatal stenosis or damaged external urinary sphincter, stress urinary incontinence, post void residual (PVR) >300 mL or urinary retention, use of self-catheterization, or prior prostate surgery, patients on anticoagulants, bladder anticholinergics or with severe cardiovascular disease. Of 17 participating trial sites in the United States, European Union, Australia, and New Zealand, 7 centers performed urodynamic studies preoperatively and at month

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6 after treatment. Urodynamic studies were optional; study centers that routinely performed UD in clinical practice included these assessments in the trial. The primary urodynamic outcome measures were detrusor pressure at maximal flow rates (PDet@Qmax), mean change in the Bladder Outlet Obstruction Index (BOOI) as a measure of BOO (BOOI = Pdet@Qmax − 2xQmax) and proportion of participants with ongoing obstruction was defined as BOOI ≥40 or BOOI between 20 and 40 with a slope gradient [(pDet@Qmax-Pvoid0)/Qmax] >2. Several additional patient-reported outcomes and other assessments were included in the study. In this manuscript, we explore relationship of UD measures to IPSS, including subscores. Differences in continuous value distributions were compared with one- or 2-sample *t* tests or Wilcoxon tests if non-normally distributed. Differences in groups across time were calculated with repeated measures analysis of variance. Proportions were compared across groups using Fisher exact tests. Changes in the proportion obstructed within individual were evaluated using McNemar's test.

RESULTS

The 7 centers performing UD enrolled and treated 83 subjects (46% of all randomized trial subjects). Compared to sites not doing UD, sites doing UD were more likely to be outside the US (P = .0072), and sites' patients had a lower frequency of touching median lobes (P < .0001) and a lower degree of median lobe obstruction (P = .0187), and the degree of bladder trabeculation was lower (P = .0012). In centers performing UD, UD studies were done in 77 of 83 (93%) of subjects at baseline and 66 of 80 (83%) of available subjects at 6 months. Of the 4 primary UD measures, there were no differences in baseline values amongst those having vs not having 6-month measures, with the exception of slightly lower baseline Qmax in subjects not having 6-month UD follow-up (6.3 vs 8.5 cc/sec, P = .0291). All analysis that follows is restricted to the 66 subjects having UD measures at both baseline and follow-up. Of the 66 analysis subjects, 43 (65%) underwent Aquablation and 23 (35%) underwent TURP; the ratio of included subjects is consistent with the study's 2:1 randomization ratio. Individual UD measures were missing in 5 subjects.

Maximal Flow Rate and PVR

At baseline, mean Qmax was depressed, PVR elevated, and pDet@Qmax increased in both groups (Fig. 1). Statistically significant and clinically important improvements occurred in all 3 parameters, with no statistical differences in change scores across

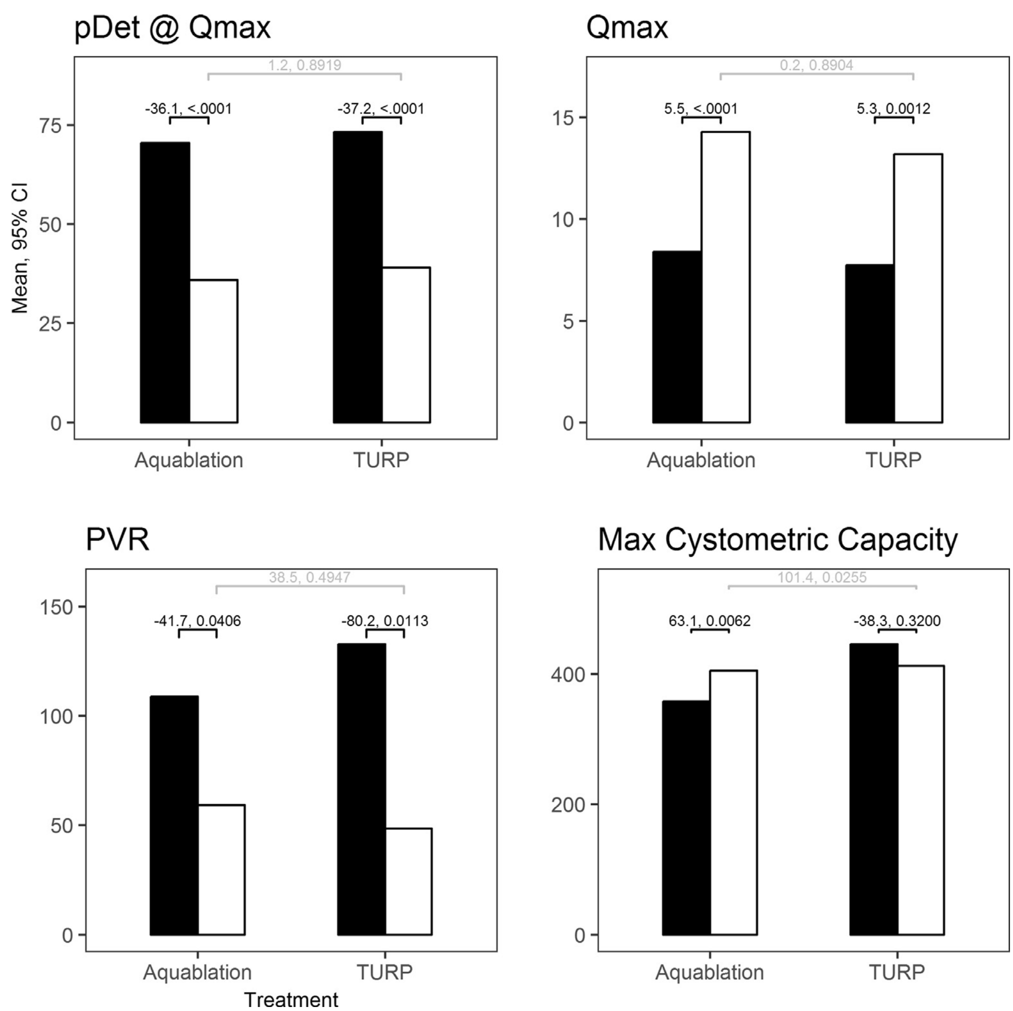

Figure 1. Improvement in UD measures by treatment and visit. Black = baseline, white = 6 months. Significance bars report effect size and P values comparing baseline and 6-month values within groups (black bars) and effect size and P value for 6-month change scores across groups (gray bars). UD, urodynamic studies.

treatment groups. A small 6-month increase in maximum cystometric capacity was seen in the Aquablation group vs a small decrease in the TURP group ($P = .0255$ for difference in change score). For Qmax, PVR, and Pdet@Qmax, the changes were clinically important in both treatment groups.

BOOI

Abrams-Griffiths (AG = pDet@Qmax-2 × Qmax), contemporarily called the BOOI, decreased markedly from baseline to 6-month follow-up in both groups with no difference in change score across treatment groups. According to the BOOI, 79% and 96% of Aquablation and TURP subjects, respectively, were obstructed at baseline ($P = .0475$ for difference); these values decreased to 22% and 22% each at 6 months (McNemar test P value < .0001 for decrease in both groups, $P = 1$ for difference in 6-month proportion across groups, Fig. 2). In the Aquablation group, subjects with BOOI suggesting obstruction had larger changes in IPSS, IPSS QOL and IPSS voiding, and storage scores compared to subjects without obstruction (Fig. 3). Score change differences over all time points were 6.5 points for change in IPSS ($P = .0096$), 1.5 points for change in IPSS QOL (.0103), 4.4 points for change in IPSS voiding ($P = .0139$), and 2 points for change in IPSS storage ($P = .0519$). In the smaller TURP group, only one subject was “not obstructed” at baseline, preventing a statistical analysis within the TURP group.

DISCUSSION

While TURP is considered the gold standard for surgical treatment of BPH, it carries risks such as bleeding, urinary incontinence, and retrograde ejaculation.[9] Alternative procedures such as Holmium (HoLEP), Thulium, Photoselective-Vaporization (PVP) and HoLEP in particular, have a growing evidence base to support their comparability to TURP.[10] Despite their growing popularity, however, these laser-based approaches have important disadvantages, namely thermal damage to the tissue beyond the target zone and a substantial learning curve.

Aquablation arose from the desire for a surgical procedure with similar efficacy to TURP but with less reliance on surgeon skill (ie, shorter learning curve) and a better safety profile. Both objectives may be attainable as a result of more precise tissue resection under image guidance and robotic control that avoids key structures related to sexual function. As Aquablation is a tissue resective technique like TURP and PVP, it was not surprising that WATER results showed similar efficacy for symptom scores, quality of life, and uroflow measures.[6] The current analysis augments the trial's findings by showing large and similar improvements in UD measures (specifically Pdet@qmax

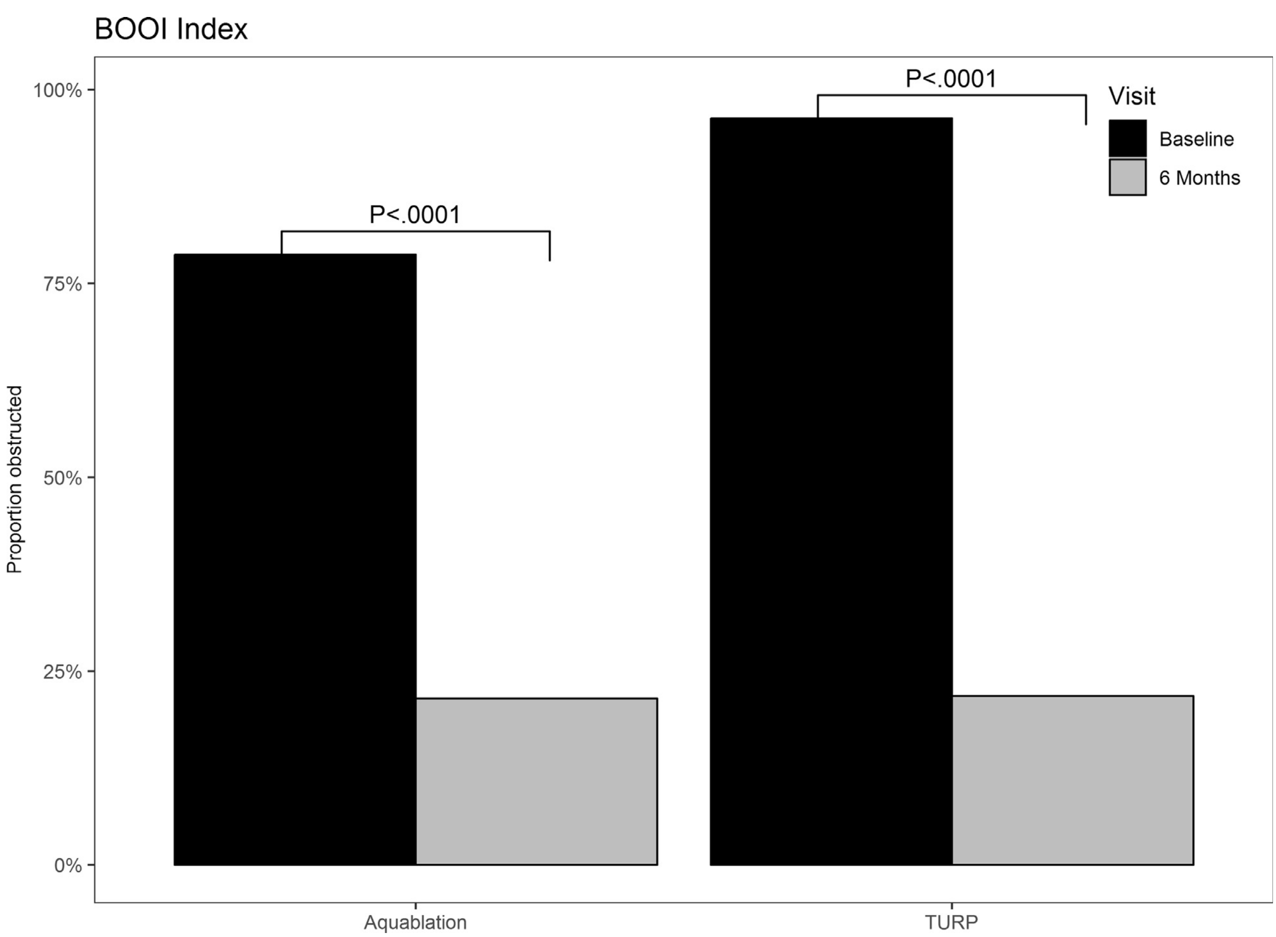

Figure 2. Change in proportion of subjects with obstruction by treatment and visit. Obstruction calculated based on BOOI. BOOI, Bladder Outlet Obstruction Index.

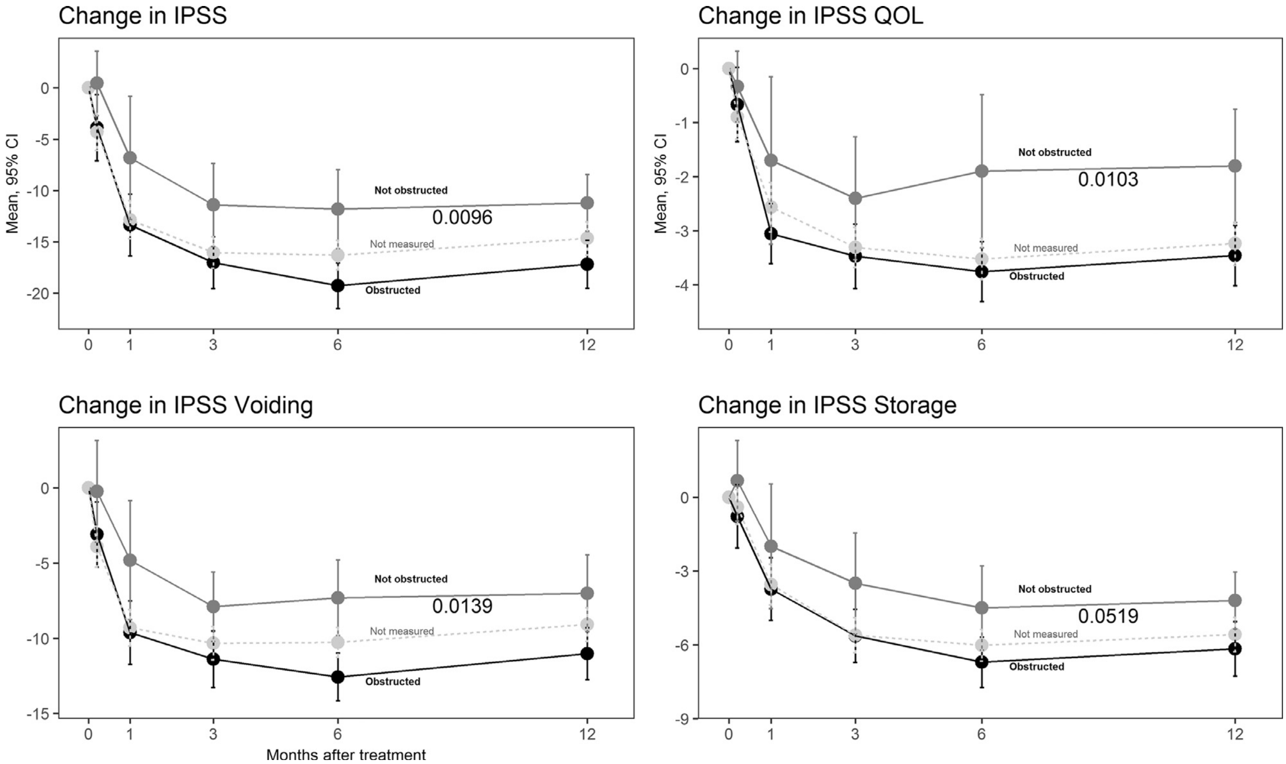

Figure 3. Impact of obstruction as measured by UD on change in IPSS, IPSS QOL, IPSS storage, and voiding subscales by visit ID. Only Aquablation cases are shown. Black line = obstructed by BOOI; dark gray line = not obstructed by BOOI; light gray dotted line = values from sites not performing UD. Numeric annotation shows repeated measures analysis of variance *P* value comparing responses in men who were obstructed vs unobstructed at baseline according to BOOI. IPSS, International Prostate Symptom Scores; QOL, quality of life.

and BOOI) in patients undergoing Aquablation or TURP. By BOOI, both treatments were highly successful in reducing measurable urinary outflow tract obstruction. UD improvements observed in our study were similar to those observed for resective procedures as determined by meta-analysis[11] (summarized in Table 1) but larger than those for nonresective procedures such as transurethral microwave thermotherapy[12] and transurethral needle ablation,[13] though the nonconcurrent nature of this comparison should be noted. Previous meta-analyses of randomized trials have also shown no statistically significant differences in Qmax improvements for other transurethral interventions, specifically PVP or Thulium laser ablation as compared to TURP.[14–17] In our study, Aquablation and TURP had comparable improvements in Qmax (~5.4 cc/sec), representing an approximate 103% increase.

Several urologic society guidelines recommend performance of UD, suggesting that these can significantly improve patient outcomes in the treatment of BPH,

Table 1. Comparison of current study to values in meta-analysis of Fusco et al[9]

Source	Treatment	Baseline IPSS*	Prostate Size	% Improvement in PdetQmax	Improvement in BOOI†	% Improvement in Qmax
Fusco	TURP	NS		49%	60	123%
	HOLEP			64%	78	179%
	PVP			51%	55	99%
	TUVP			53%	64	107%
	TUNA			31%	40	80%
	TUMT			24%	34	77%
Current study	Aquablation	23.7 (6.1)	53 (14.6)	51%	48	102%
	TURP	21.9 (6.4)	53.8 (13.5)	45%	48	106%

BOOI, Bladder outlet obstruction Index; HOLEP holmium laser enucleation of the prostate PdetQmax detrusor pressure at Qmax; NS = not stated; PVP, photoselective vaporization of the prostate; Qmax maximum urinary flow rate; TUMT transurethral microwave thermotherapy; TUNA, transurethral needle ablation; TURP, transurethral resection of the prostate; TUVP, transurethral electrovaporization of the prostate.
* Mean (SD).
† BOOI = PdetQmax − 2Qmax.

particularly for invasive therapies such as surgery.[7,18] Elevated BOOI predicts larger improvements in IPSS scores and flow rates after TURP[19] and we observed similar findings after Aquablation (Fig. 3). The difference in response rates between those with and without obstruction was clinically important (5-point difference in IPSS change score and a 1.5-point difference in IPSS QOL). While UD studies may aid in identifying patients who may be unsuitable for surgery, subjects in our study with low BOOI ("not obstructed") had smaller, but still clinically meaningful changes in IPSS scores and subscores. Although international associations' recommendations vary regarding the role of UD in diagnostic work-up for LUTS, all seem to agree that UD are indicated for patients with suspected neurologic contribution to LUTS, evaluation of the need for retreatment in patients with symptom recurrence after surgery, and patients with non-diagnostic noninvasive testing and residual uncertainty regarding the contribution of BOO to LUTS.[20]

Previous reports from this study included primarily symptom scores and uroflow measures. The current report provides further objective evidence to support the use of Aquablation in clinical practice through showing UD equivalence to TURP. In our study, Aquablation subjects were less likely to be obstructed by BOOI at baseline compared to TURP subjects. Since obstruction predicts larger symptom score responses,[20] including, in our study, IPSS, IPSS QOL, and IPSS subscore responses, it is possible that symptom score reductions after Aquablation in our trial may be somewhat understated compared to TURP.

The main strengths of our trial are its blinded, prospective, randomized multicenter design. Limitations of our study include the following. Because UD were optional in WATER, our analysis had limited subjects at the 7 sites performing such evaluations in the trial, which could have introduced a bias. While sample size was large enough to detect statistically significant and clinically important changes from baseline in each group, it is possible that smaller differences in UD responses across treatment groups might not be detectable due to limited sample size. Moreover, some bias might be introduced by the 83% 6-month UD follow-up compliance rate.

CONCLUSIONS

In this trial, improvements after Aquablation in objective measures of bladder outlet obstruction were similar to those observed after TURP. The degree of improvement after Aquablation appears comparable to those after other transurethral interventions such as HOLEP, Thulium, and PVP.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urology.2019.01.020.

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