Men with lower urinary tract symptoms secondary to BPH undergoing Aquablation with very large prostates (> 150 mL)

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Introduction: *The AUA guidelines for benign prostatic hyperplasia distinguish treatments based upon prostate volume (PV), particularly for very large prostates (> 150 mL). While the clinical outcomes and benefits of Aquablation have been studied for men with average and large prostates, it is unknown whether this technology can be used for very large prostates.*

Materials and methods: *Men with PV > 150 mL undergoing Aquablation were identified retrospectively from four North American hospitals. The surgical times and clinical outcomes of men with very large prostates (> 150 mL) were compared to data from men with average PV ≤ 80 mL (WATER study) and large PV 80 mL-150 mL (WATER II study).*

Results: *The average PV of men who underwent Aquablation with very large prostates was 209 mL ± 56 (n = 34, range 151-362 mL), large PV 107 mL ± 20 (n = 101, range 80-150 mL) and average PV 54 mL ± 16 (n = 116, range 30-80 mL). For men with PV > 150 mL, baseline IPSS was 19 ± 6. With a mean follow up of 7 ± 9 months, the IPSS improved to 7 ± 5 (p < 0.001). Peak urinary flow rate, Qmax, improved from 7 ± 4 mL/s to 19 ± 5 mL/s (p<0.001). Compared to the two other PV groups, there were no differences in terms of improvements in IPSS, quality of life, or uroflowmetry. There were no reports of transfusions (0%) in the cohort of men with very large prostates.*

Conclusions: *In the present study, we demonstrate that Aquablation is effective and safe in prostates greater than 150 mL while showing consistent outcomes compared to average and large prostates sizes.*

Key Words: Aquablation, BPH, LUTS, prostate surgery, robotics, urology

Introduction

Benign prostatic hyperplasia (BPH) contributes to the development and progression of lower urinary tract symptoms (LUTS) in aging men. Specifically, it has been estimated that 90% of men will develop LUTS, and 50% of them will experience moderate-to-severe symptoms by the time they are 85 years old. Symptoms associated with BPH negatively impact a man's quality of life[1,2] and contribute to a large economic healthcare burden.[3]

Within the past decade, there has been an increasing number of medical and surgical options for the treatment of LUTS secondary to BPH. Patient selection

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for the appropriateness of each treatment option is influenced by many variables including prostate size, anatomic variations (e.g. median lobe), predominant urinary symptom, desire for preservation of sexual function, need for anticoagulation, etc. The AUA guidelines for BPH recommend a volume estimate study prior to intervention. This recommendation is based in part on the concept that different surgical treatment options may be efficacious for men with different shaped and sized prostates. Only a limited number of technologies are appropriate for men with large (80-150 mL) and very large prostates (> 150 mL).[4]

The robotically executed waterjet-based resection of the prostate (Aquablation procedure) is an established technology that is included in authoritative guidelines as a treatment for men suffering from BPH. Prospective randomized controlled trials have compared Aquablation to transurethral resection of the prostate and documented similar safety profiles and effectiveness for improving LUTS in men with small-to-average sized prostates (30-80mL; WATER study)[5] and large prostates (80-150mL; WATER II study).[6,7] However, because of the ability to contour treatment plans based upon the size and shape of the prostate, Aquablation has superior ability to preserve sexual function.

There are only a few technologies that have been traditionally offered and studied for men with very large prostates are limited. Simple enucleation, whether performed open or laparoscopically/robotically, is invasive and inherently carries additional surgical risks and recovery times.[8,9] While laser enucleation procedures (e.g. holmium laser enucleation of prostate) are performed endoscopically, they are limited by the steep surgical learning curve[10] and somewhat prolonged recovery periods that can be plagued by stress and urge incontinence[11]. In addition, none of the techniques offer preservation of anterograde ejaculation in a high frequency of men. Aquablation potentially offers a solution to many of these issues for men with very large prostates.

Materials and methods

Aquablation therapy performed by the AquaBeam System (PROCEPT BioRobotics, Redwood City, CA, USA) has been previously described.[12] Prior to the procedure all anticoagulation medications were stopped before surgery and were not restarted for approximately 3-4 days postoperatively based upon physician preferences. With real-time prostate visualization, the surgeon uses the planning software on the conformal planning unit (CPU), the monitor screen, to mark the target resection contour. Under the surgeon's control, the ablation of tissue is robotically executed using a high-velocity waterjet to resect adenomatous tissue while avoiding the verumontanum and the ejaculatory ducts. Hemostasis is then performed using a focal bladder neck cautery technique.[13] Based upon prostate size and shape, treating physicians may use several passes of the waterjet to remove obstructing adenoma. This is particularly relevant for men with very large prostates.

Four hospitals utilizing Aquablation retrospectively gathered and combined data for patients with prostate volumes (PV) > 150 mL. Standard BPH outcomes variables were collected: PV, operative time, transfusions, Clavien-Dindo I persistent events (incontinence, erectile dysfunction, ejaculatory dysfunction), International Prostate Symptom Score (IPSS), and Qmax. Data reported as mean ± standard deviation. For comparison to average PV (≤ 80 mL), data from the WATER study was used, NCT02505919. For comparison to large PV (80-150 mL), data from the WATER II study was used, NCT03123250. Comparison data of 6 months follow up was documented for men in all groups. Statistical analyses comparing intraoperative and clinical outcomes were made using R.

Results

Thirty-four patients with LUTS secondary to BPH with very large prostates were evaluated. The mean age was 69 ± 8 (range 54-83) with an average PV of 209 mL ± 56 (range 151-362 mL). As comparison groups, men historically enrolled in two previous FDA Aquablation controlled trials were enrolled including 101 men with large- and 116 men with average-size prostates. Men with very large prostates were slightly older than men with average- and large-size prostates ($p = 0.037$; Table 1). Mean PSA value increased with increasing PV ($p < 0.001$; Table 1). The mean operative time for men with very large prostates was 64 ± 24 minutes (range 31-140), and mean operative time increased slightly with increasing PV ($p < 0.001$; Table 1).

There were no reports of transfusions (0%) in the cohort of men with very large prostates and most patients were discharged POD1. These results aligned with the average and large cohorts except a higher transfusion was observed in the large PV cohort from WATER II ($p = 0.04$).

Men with very large prostates reported severe LUTS as measured by the IPPS (mean 19 ± 6). With a mean follow up of 7 ± 9 months, IPSS improved to 7 ± 5 ($p < 0.001$), Figure 1. Peak urinary flow rate (Qmax) improved from 7 ± 4 mL/s to 19 ± 5 mL/s ($p < 0.001$), Figure 1. Clinical outcomes were similar regardless

TABLE 1. **Summary of demographic, procedure, preoperative, and postoperative data from average, large, and very large prostates undergoing Aquablation.**

	Average (≤ 80 mL)	Large (80-150 mL)	Very large (> 150 mL)	p value*
N	116	101	34	
Age, years	66 ± 7	68 ± 7	69 ± 8	0.037
Prostate volume, mL	54 ± 16	107 ± 20	209 ± 56	< 0.001
Procedure				
Operative time, minutes	40 ± 15	55 ± 19	64 ± 24	< 0.001
Periprocedural Transfusion, n (%)	1 (0.9%)	6 (5.9%)	0 (0%)	0.04
Preoperative				
IPSS	23 ± 6	23 ± 6	19 ± 6	0.002
QoL	5 ± 1	5 ± 1	4 ± 1	< 0.001
Qmax, cc/sec	9 ± 3	9 ± 3	7 ± 4	0.003
PSA (ng/mL)	3.7 ± 3	7.1 ± 5.9	8.7 ± 5.9	< 0.001
Postoperative (6 months)				
IPSS	6 ± 5	6 ± 5	7 ± 5	0.56
QoL	1 ± 1	1 ± 2	1 ± 1	1
Qmax, cc/sec	20 ± 11	19 ± 11	19 ± 5	0.74
PSA (ng/mL)	2.5 ± 2	3.9 ± 3.8	5.7 ± 4.8	< 0.001

*ANOVA used for all data comparisons except transfusion data where Chi-Square method was used.
IPSS = International Prostate Symptom Score.

of PV, (p = 0.56 for postoperative IPSS; p = 0.74 for postoperative Qmax; Table 1). There were no reports of incontinence, erectile dysfunction, or ejaculatory dysfunction in the very large PV cohort. PSA levels decreased similarly in each group (32% average, 45% large, 35% very large PV). Two of the patients in the very large PV group had low grade prostate cancer documented on submitted pathologic tissue.

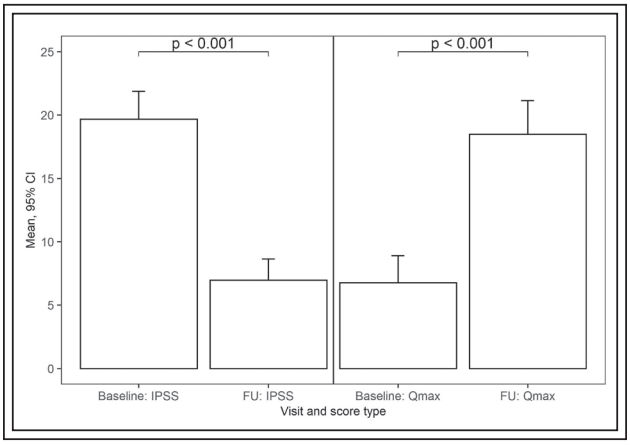

Figure 1.IPSS and Qmax results for very large prostates

Discussion

Aquablation has been shown to be safe and effective in PV up to 150 mL in three distinct clinical studies; WATER,[14] WATER II,[15] and OPEN WATER.[16] Both WATER and WATER II were FDA studies with data reported out to 3-year follow up. In those studies, clinical improvement was similar to the gold standard TURP in regard to improvement of LUTS (as measured by IPSS) as well as Qmax in prostate sizes of 30-80 cc. For larger PV (> 80 mL), similar clinical outcomes were achieved without an equivalent comparison. What makes Aquablation unique is the limited irreversible side effects of ejaculatory dysfunction, erectile dysfunction and incontinence. These results were further confirmed in meta-analysis publication where data was grouped by the following: PV < 100 mL, PV ≥ 100 mL, prostate anatomy with an obstructive median lobe identified by imaging, and prostate anatomy without an obstructive median lobe. The meta-analysis concluded that regardless of prostate size or anatomical shape, Aquablation therapy by using real-time imaging and robotic execution can maximize efficacy and minimize irreversible complications.[17] The results of the present study support that Aquablation is a suitable

technology associated with similar improvements in LUTS for men with very large prostates.

A striking result of the present data was the significantly lower rate of significant bleeding among the cohort of men with very large PV, as measured by the frequency of blood transfusions. This was likely related to the focal bladder neck cautery technique which was used in the present study for all men but not utilized in the other groups, including WATER II, based upon historic data. Elterman et al previously reported this technique in detail demonstrating that the larger the prostate size is, the higher the risk of transfusion when cautery is not used.[18] Implementation of this technique was initiated in January 2020 and has now been utilized in more than 2,000 consecutive procedures in a non-study trial setting where the mean prostate size was 87 mL (range of 20-363 mL) and the transfusion rate was 0.8%.[13]

While the overall operative times were significantly higher for men within the very large prostate group, this was not necessarily clinically significant (i.e. only increased by approximately 10 and 20 minutes when compared to men within the large and average size prostate groups). This increase is likely explained by the additional time to perform focal bladder neck cautery which adds an average of 12 minutes to the procedure. As mentioned, this technique was not utilized in the FDA trials (WATER, WATER II). However, even if this technique truly adds additional time for men with very large prostates, it is not proportional to the increase in PV. Many other endoscopic techniques including bipolar transurethral resection, photo-vaporization, and laser enucleation increase operating room time proportionally to PV.[19] However, this is not the case for Aquablation, and thus, this technique provides reproducible results in a relatively uniform time, regardless of prostate size or shape.

It is notable that Aquablation had significant improvements in overall LUTS, regardless of PV. It has previously been shown that men undergoing Aquablation with large prostates are slightly more susceptible to transient postoperative urgency and urge incontinence.[17] Importantly, no patient in any cohort, including the very large size PV cohort, exhibited stress incontinence. This is in stark contrast to other techniques including holmium laser enucleation and simple enucleation (robotic or open) that have been associated with temporary or permanent stress incontinence.[11,20]

There are several limitations for this study which include the fact that our study comparator groups were derived from historic, controlled clinical trial groups. As such, operating room times and techniques may reflect differences in techniques and learning curves since the trials were conducted. Also, the number of men within the very large prostate cohort is relatively small, and additional studies involving more men should be performed to validate the present results. In addition, the length of follow up for the very large cohort is less than 1 year. As such, the long term durability remains to be reported. However, if prostate volume removed can be approximated based upon the overall percent decrease in PSA values, we would expect that all groups have a similar proportion of adenoma resected and would therefore hypothesize similar retreatment rates per group. Since the Aquablation re-treatment rates for men with average and large PV is ~1% annually, similar rates in men with very large PV would support a durable response in the long term. Taken together, Aquablation offers a safe and clinically effective treatment for men with LUTS secondary to a very large prostate.

Conclusions

In the present study, we demonstrate that Aquablation is effective and safe in prostates greater than 150 mL while showing consistent outcomes compared to average and large prostates sizes.

Disclosures

Drs. Helfand, Kasraeian, Sterious, and Elterman have had or currently have a consulting agreement with PROCEPT BioRobotics. No funding was received for this manuscript. □

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