# Interventional procedure overview of transurethral water-jet ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia

## Contents

**Table 1 Abbreviations**

| Abbreviation | Definition |
|---|---|
| BPH | Benign prostatic hyperplasia |
| HoLEP | Holmium laser enucleation of the prostate |
| IIEF | International Index of Erectile Function |
| IPSS | International Prostate Symptom Score |
| ISI | Incontinence severity index |
| LUTS | Lower urinary tract symptoms |
| MAUDE | Manufacturer and User Facility Device Experience |
| MSHQ | Male Sexual Health Questionnaire |
| MSHQ-EjD | Male Sexual Health Questionnaire – ejaculatory dysfunction |
| SD | Standard deviation |
| TRUS | Transrectal ultrasound |
| TURP | Transurethral resection of the prostate |
| PSA | Prostate specific antigen |
| PVR | Post void residual |
| Qmax | Maximum urinary flow rate |
| QoL | Quality of life |

## Indications and current treatment

Benign prostatic hyperplasia is a common condition that affects older people with a prostate. Stromal and epithelial cells increase in number, causing the prostate to get bigger. It often happens in the periurethral region of the prostate, with large discrete nodules compressing the urethra. Symptoms include hesitancy during urination, interrupted or decreased urine stream (volume and flow rate), nocturia, incomplete voiding and urinary retention.

Mild symptoms are usually managed conservatively. Drugs may also be used, such as alpha-adrenoceptor blockers and 5-alpha-reductase inhibitors. If other treatments have not worked, there are a range of surgical options that may be considered including TURP, transurethral vaporisation, holmium laser enucleation, insertion of prostatic urethral lift implants, prostatic artery embolisation or prostatectomy (see NICE's guideline on lower urinary tract symptoms in men). Potential complications of some of these surgical procedures include bleeding, infection, urethral strictures, incontinence and sexual dysfunction.

## Unmet need

Bothersome lower urinary tract symptoms caused by BPH are a major burden for the ageing population occurring in up to 30% of people older than 65 years with a prostate. There are a number of established and effective medical and surgical treatments for BPH but potential complications of some of the surgical procedures include bleeding, infection, urethral strictures, incontinence and sexual dysfunction. There is a need for surgical treatments which are as effective as established treatment but have a reduced frequency of these complications.

This procedure is potentially suitable for all prostate sizes and to be done as a day case procedure. Professional experts noted that this procedure may be of particular benefit for people with larger prostates for whom alternative treatments that aim to protect sexual function are inappropriate because of prostate size or shape or other factors, such as chronic urinary retention.

## What the procedure involves

Transurethral water-jet ablation for lower urinary tract symptoms caused by BPH uses a specialised system that combines image guidance and robotics for the targeted removal of prostate tissue. The procedure is usually done under general or spinal anaesthesia. Transrectal ultrasound is used throughout the procedure. A handpiece with an integrated cystoscope and ablation probe is inserted through the urethra and into the bladder. When it is correctly positioned, planning software is used to create a personalised treatment plan. A high-speed jet of saline is then delivered to the prostate at various flow rates, to give targeted and controlled tissue removal, according to the treatment plan. The ablated tissue is aspirated through ports in the handpiece and can be used for histological analysis. Several methods are used to control bleeding, including cautery, a balloon catheter in the bladder (with or without bladder neck traction) and a balloon catheter in the prostatic fossa. After the procedure, a 3-way Foley catheter is placed through the penis into the urethra and the bladder is continuously irrigated. The catheter is removed before discharge from hospital, usually on the day after the procedure.

A possible advantage of the procedure is the potential to preserve sexual function. The procedure does not use heat to ablate the prostate tissue, which removes the risk of complications arising from thermal injury.

## Outcome measures

The main outcomes included IPSS, Qmax, PVR, PSA, retreatment rates and adverse events. Some of the measures used are detailed in the following paragraphs.

### IPSS

The IPSS is a validated questionnaire often used to assess symptoms of BPH (it is also referred to as the American Urological Association BPH Symptom Score Index). It includes questions on incomplete bladder emptying, frequency, intermittency and urgency of urination, weak urine stream, straining to urinate and nocturia. Higher scores represent worse symptoms. In general, an IPSS symptom score of 0 to 7 indicates mild symptoms, 8 to 19 indicates moderate symptoms and 20 to 35 indicates severe symptoms. An additional question asks the respondent how they feel about their BPH symptoms and the response yields a score for quality of life (ranging from 0 to 6, with 0 representing ‘delighted’ and 6 representing ‘terrible’).

### Qmax

In uroflowmetry, Q refers to the volume of fluid expelled by the urethra per unit time (flow rate). Qmax is the maximum measured value of the flow rate after correction for artefacts. It decreases with age and voided volume. A low Qmax value is commonly a sign of obstruction.

### IIEF

The IIEF is a 15-item questionnaire used to assess male sexual function in 5 domains: erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction. Each domain has its own score range and lower scores represent greater dysfunction:

- Erectile function score: range 0 to 30 (scores of 24 or less represent increasing dysfunction)
- Orgasmic function score: range 0 to 10 (scores of 8 or less represent increasing dysfunction)
- Sexual desire score: range 0 to 10 (scores of 8 or less represent increasing dysfunction)
- Intercourse satisfaction score: range 0 to 15 (scores of 12 or less represent increasing dysfunction)

- Overall satisfaction score: range 0 to 10 (scores of 8 or less represent increasing dysfunction).

**ISI**

The ISI is a questionnaire composed of 2 items which assess the frequency (4 levels) and amount (3 levels) of urine leakage. The index value (1 to 12) is reached by multiplying the 2 items.

**MSHQ-EjD**

The MSHQ-EjD includes 3 questions relating to ejaculation dysfunction, including completeness of ejaculation, strength of ejaculation and volume of semen on ejaculation. Each question is scored 0 to 5, with lower scores indicating worse sexual function. An additional question measures how much the patient is bothered by his ejaculatory function on a scale from 0 to 5, with a higher score indicating greater bother.

# Evidence summary

## Population and studies description

This interventional procedures overview is based on approximately 3,300 people from 1 systematic review (Chen 2023), 1 pooled analysis of 4 trials (Elterman 2021), 1 randomised controlled trial reported in 2 publications (the trial is also included in the systematic review and pooled analysis; Gilling 2020 and 2022), 1 prospective multicentre single-arm trial reported in 2 publications (the trial is also included in the pooled analysis; Zorn 2021 and Bhojani 2023), 1 retrospective cohort study (Helfand 2021), 1 retrospective non-randomised comparative study (Gloger 2021) and 2 retrospective case series (1 of which also included data from the 4 trials in the pooled analysis; Elterman 2021 and 2020). There was also a report from the FDA MAUDE database (Kaplan-Marans 2021). There is some patient overlap between the studies. This is a rapid review of the literature, and a flow chart of the complete selection process is shown in figure 1. This overview presents 11 studies as the key evidence in table 2 and table 3, and lists 55 other relevant studies in table 5.

The 11 key studies included data from Europe, Asia and North America and treatment dates ranged from 2014 to 2021.

The systematic review by Chen et al. (2023) included 7 studies with 551 people. Of the 7 studies, 6 were prospective (including 1 randomised controlled trial) and 1 was a retrospective review of prospectively collected data. The study populations were heterogeneous and there was variation in the outcome measures. In addition, the studies reported outcomes at inconsistent time points after the procedure.

The pooled analysis by Elterman et al. (2021) included 425 men with moderate to severe LUTS attributable to BPH. Data on water-jet ablation was analysed from 1 randomised controlled trial (WATER), 2 prospective multicentre single-arm trials (WATER II and FRANCAIS WATER) and a prospective multicentre observational study (OPEN WATER), all of which had at least 1 year follow up. Prostate size varied between the 4 studies and ranged from 20 to 150 ml. Publications with longer term outcomes for WATER and WATER II have been included separately in table 2 and table 3 (Gilling 2020 and 2022, Zorn 2021 and Bhojani 2023).

In the WATER trial, 181 men with prostate size between 30 and 80 ml were randomised to have either water-jet ablation (n=116) or TURP (n=65). Outcomes were reported at 3 and 5 years follow up. Patients and follow-up assessors were blinded to treatment assignment up to 3 years, at which point patients were unblinded. The authors noted that the 4-year and 5-year follow-up visits were during the pandemic caused by COVID-19 and longer-term outcomes were available for fewer men than anticipated (50% of men in the water-jet group and 49% in the TURP group had 5-year follow-up data; Gilling 2020 and 2022).

The WATER II trial was a prospective multicentre single-arm trial including 101 men with prostate size between 80 and 150 ml (3-year follow up was complete for 78 men and 5-year follow up was complete for 60 men; Zorn 2021 and Bhojani 2023).

The study by Kaplan-Marans et al. (2021) was a comparison of device-related adverse events in the FDA MAUDE database associated with 3 procedures used to treat BPH (water-jet ablation, prostatic urethral lift and transurethral water-vapour therapy). A total of 391 adverse events were described between 2015 and 2020. The MAUDE database includes mandatory reports from manufacturers and device importers when a device may have caused injury to a patient, and voluntary reports from other sources, including healthcare professionals and patients. Limitations of the database include under-reporting, duplicate reporting, incomplete reports and uncertainty if the device caused the complication being described. The true denominator for these events is not captured and the database is not designed to calculate or compare complication rates.

The study by Helfand et al. (2021) was a retrospective cohort study of 251 men, comparing outcomes for different size prostates. A group of 34 men with very large prostates (defined as more than 150 ml) were compared with men with large (n=101) or average size (n=116) prostates who were included in the WATER and WATER II studies. The mean follow up for the men with very large prostates was 7 months.

The study by Gloger et al. (2021) was a retrospective, single centre non-randomised comparative study including 167 men who had water-jet ablation with subsequent selective bipolar cauterisation and 215 men who had HoLEP. The primary aim of the study was to assess the risk of perioperative bleeding complications. Two other retrospective studies also focused on perioperative bleeding and strategies for its management. One was a case series of 2,089 men with prostate size ranging from 20 to 363 ml (Elterman 2021b), all of whom had non-resective focal cautery at the bladder neck after water-jet ablation. The other was a case series of 801 men, including data from the 4 trials described in the pooled analysis, which compared transfusion rates between different haemostasis methods (Elterman 2020).

Table 2 presents study details.

**Figure 1 Flow chart of study selection**

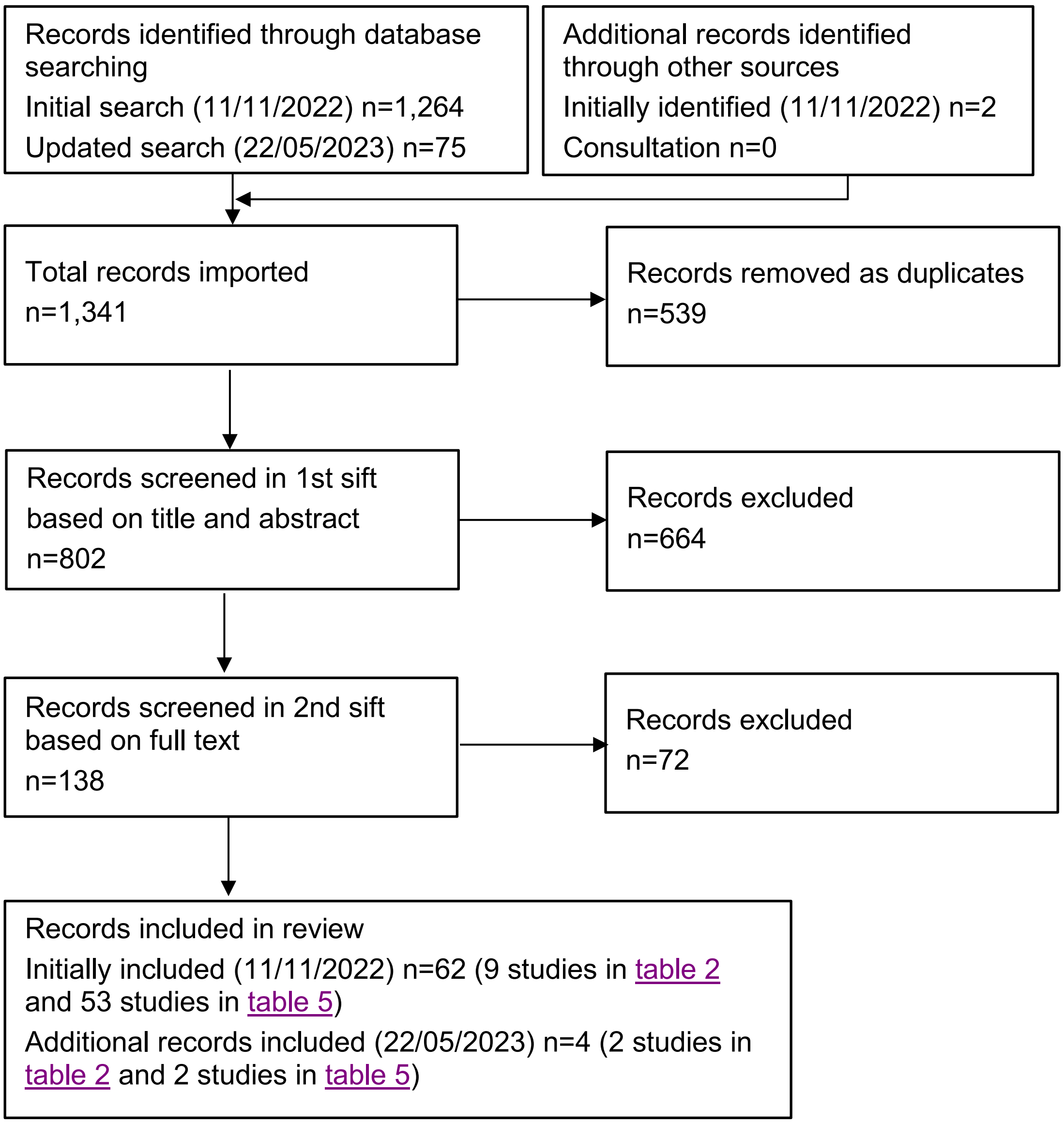

**Table 2 Study details**

| Study no. | First author, date<br>country | Patients | Mean age (years) | Study design | Inclusion criteria | Intervention | Follow up |
|---|---|---|---|---|---|---|---|
| 1 | Chen D, 2023<br>UK, Germany, Australia, New Zealand, Lebanon, India, US, Canada, France | n=551 | not reported | Systematic review, including 7 studies.<br>Search date: August 2021 | Studies that analysed ablation outcomes in men with BPH were included in the analysis. Study designs considered for inclusion included randomised clinical trials, prospective studies, and retrospective cohort studies. Restrictions including English language publications and a minimum sample size of 10 patients were used. | Water-jet ablation using AQUABEAM System (PROCEPT BioRobotics, US). | 3 months to 2 years |
| 2 | Elterman D, 2021a<br>US, UK, Australia, New Zealand, Canada, France, Germany, Lebanon | n=425 | not reported for whole cohort | Pooled analysis of 4 trials (WATER, WATER II, FRANCAIS WATER, OPEN WATER). | Prospective multicentre studies of water-jet ablation with at least 1 year follow up. All men had moderate to severe LUTS caused by BPH and prostate size | Only results for water-jet ablation (n=425) were analysed.<br>Device: AQUABEAM robotic system | 1 year |

| Study no. | First author, date<br>country | Patients | Mean age (years) | Study design | Inclusion criteria | Intervention | Follow up |
|---|---|---|---|---|---|---|---|
| | | | | Study dates were between 2015 and 2019. | ranged from 20 to 150 ml. | (PROCEPT BioRobotics, US) | |
| 3, 4 | Gilling P, 2020 and 2022<br>US, UK, Australia, New Zealand | n=181<br>Mean prostate size 53 ml | 66 | Randomised controlled trial (WATER trial).<br>Enrolment was between 2015 and 2016. | Men aged 45 to 80 years with a prostate size 30 to 80 ml, moderate to severe symptoms (IPSS 12 or higher) and Qmax less than 15 ml/second. | • Water-jet ablation (n=116)<br>• TURP (n=65)<br>Device for water-jet ablation: AQUABEAM (PROCEPT BioRobotics, US) | 3 and 5 years |
| 5, 6 | Zorn K, 2021; Bhojani N, 2023<br>US, Canada | n=101<br>(78 with 3-year follow up, 60 with 5-year follow-up)<br>Mean prostate size 107 ml | 68 | Prospective multicentre single-arm trial (WATER II).<br>Enrolment was in 2017. | Men aged 45 to 80 were included if they had a prostate volume between 80 and 150 ml by TRUS, baseline IPSS 12 or higher, Qmax less than 15 ml/second, a serum creatinine less than 2 mg/dl, a history of inadequate or failed response to medical therapy and mental capability, and willingness to participate in the study. | Water-jet ablation using AQUABEAM (PROCEPT BioRobotics, US).<br>For larger prostates, 2 passes of the AQUABEAM probe were typically used. Catheter traction was held for an average of 18 hours.<br>Electrocautery was not used for haemostasis in | 3 and 5 years |

| Study no. | First author, date country | Patients | Mean age (years) | Study design | Inclusion criteria | Intervention | Follow up |
|---|---|---|---|---|---|---|---|
| | | | | | Men were excluded if they had body mass index 42 kg/m$^2$ or higher, a history of prostate or bladder cancer, clinically significant bladder calculus or bladder diverticulum, active infection, previous urinary tract surgery, urinary catheter use daily for 90 or more days, chronic pelvic pain, diagnosis of urethral stricture, meatal stenosis or bladder neck contracture, use of anticholinergic agents, and other general conditions that could prevent adequate study follow up. Men with urinary retention were excluded if the catheter was in place for more than 90 days. | any of the procedures. | |

| Study no. | First author, date<br>country | Patients | Mean age (years) | Study design | Inclusion criteria | Intervention | Follow up |
|---|---|---|---|---|---|---|---|
| 7 | Kaplan-Marans E, 2021<br>US | 391 adverse events (102 for water-jet ablation) | Not reported | Registry (MAUDE database).<br>Reports between 2015 and 2020 were included. | The MAUDE database was queried using the terms ‘Aquabeam’, ‘Rezum’ and ‘UroLift’ for adverse events reported between January 2015 and July 2020. | • Water-jet ablation (102 events)<br>• Prostatic urethral lift (132 events)<br>• Transurethral water-vapour therapy (157 events) | Not reported |
| 8 | Helfand B, 2021<br>US, Canada | n=251 (34 with very large prostates, 101 with large and 116 with average size prostates) | 69 for men with very large prostates | Retrospective cohort study, comparing outcomes for different size prostates. | Men with prostates larger than 150 ml (defined as very large) were compared with men with large or average size prostates who were included in the WATER or WATER II studies. | Water-jet ablation.<br>Device: AQUABEAM system (PROCEPT BioRobotics, US). | 6 months (mean 7 months in group with very large prostates) |
| 9 | Gloger S, 2021<br>Germany | n=382<br>Mean prostate size 56 ml (water-jet ablation) and 95 ml | 64.7 for water-jet ablation, 70.8 for HoLEP, p<0.001 | Retrospective single centre, non-randomised comparative study.<br>Procedures were done between 2018 and 2020. | Men who had water-jet ablation between 2018 and 2020 were compared with men who had HoLEP at the same centre during the same period. The first 20 men to have water-jet ablation were | • Water-jet ablation with subsequent selective bipolar cauterisation (n=167) | 6 weeks |

| Study no. | First author, date country | Patients | Mean age (years) | Study design | Inclusion criteria | Intervention | Follow up |
|---|---|---|---|---|---|---|---|
| | | (HoLEP); p<0.001 | | | excluded to take account of the learning curve. | • HoLEP (n=215)<br>Device for water-jet ablation: AQUABEAM system (PROCEPT BioRobotics, US). | |
| 10 | Elterman D, 2021b<br>11 countries (Asia, Europe, North America) | n=2,089<br>Mean prostate size 87 ml | Not reported | Retrospective case series.<br>Procedures were done between 2019 and 2021. | Consecutive patients who had water-jet ablation between 2019 and 2021. Prostate size ranged from 20 to 363 ml. | Water-jet ablation followed by non-resective focal cautery at the bladder neck.<br>Device: AQUABEAM system (PROCEPT BioRobotics, US). | Not reported |
| 11 | Elterman D, 2020 | n=801<br>Mean prostate size 67 ml (range 20 to 280 ml) | Not reported | Retrospective case series (including data from WATER, WATER II, FRANCAIS WATER and OPEN WATER). | Data from 7 clinical studies, sponsored by PROCEPT BioRobotics, along with 4 high-volume early commercial users of the technology were included. The procedures were done | Water-jet ablation with different haemostasis techniques. Method of traction was defined as robust (using a catheter-tensioning device) or standard (taping the catheter to the | Not reported |

| Study no. | First author, date<br>country | Patients | Mean age (years) | Study design | Inclusion criteria | Intervention | Follow up |
|---|---|---|---|---|---|---|---|
| | | | | Procedures were done between 2014 and 2019. | between 2014 and early 2019. | leg, gauze knot synched up to the meatus, or no traction at all).<br>Device: AQUABEAM system (PROCEPT BioRobotics, US). | |

**Table 3 Study outcomes**

| First author, date | Efficacy outcomes | Safety outcomes |
|---|---|---|
| Chen D, 2023 | **IPSS (7 studies)**<br>At 3 months after treatment, the raw mean difference from baseline was -16.5 (95% CI, -15.3 to -17.7; p<0.001, $I^2$=75%).<br>From the available data, improvements in IPSS were sustained at 12 months.<br><br>Overall pooled effect size=10.95 (95% CI 10.0 to 11.9; p<0.001) from baseline to 3 months, $I^2$=9%. These changes were sustained for 12 months in this meta-analysis.<br><br>**Quality of life (IPSS-QoL score)**<br>The preoperative QoL score was 4.63, which led to a significantly improved pooled estimate of 1.29 at 3 months, $I^2$=51%, 7 studies. | **Perioperative outcomes**<br>Reoperation rates for haematuria and other bleeding complications needing return to theatre were reported in 3 studies, ranging from 0% to 7.9%.<br><br>**Postoperative outcomes**<br>Postoperative complications including haematuria and urinary retention were the most common. Of the 551 men included in the study, 2.9% returned to the theatre for haemostasis.<br><br>6 studies reported postoperative infection rates ranging from 2.12% to 10%.<br>Incontinence was reported in 2 studies, with rates of 0.6% to 4.9%.<br><br>Significant adverse events that happened postoperatively, if not defined, were classified as Clavien-Dindo grade 2 and greater. Five studies reported Clavien-Dindo grade 2 and grade 3 events ranging from 3.4% to 13.9%. No deaths were associated with the procedure.<br><br>**Sexual function outcomes** |

| First author, date | Efficacy outcomes | Safety outcomes |
|---|---|---|
| | | The overall MSHQ change pooled effect size was -0.6 (95% CI -1.6 to 0.5; p=0.321) before and after intervention at 3 months, $I^2$=74.5%, 4 studies. |
| Elterman, 2021 | **Mean procedure time**, defined as TRUS insertion to urinary catheter placement, was 40 minutes (median 38, range 8 to 111 minutes).<br><br>**Mean improvement in IPSS from baseline to 1 year=16 points** There was no variation across studies and 1-year scores were independent of baseline scores.<br><br>**Mean IPSS QoL improved from 4.7 at baseline to 1.4 at 1 year.** There was no variation in baseline IPSS QoL or 1-year change score across studies.<br><br>**Mean Qmax at 1 year was 20.5 ml/second, an improvement of 9.4 ml/second from baseline.**<br>The 1-year change was independent of studies.<br><br>**Mean improvement in PVR at 1 year=62 ml (median 41 ml)**<br>The improvement in PVR was strongly dependent on baseline PVR and was largest in the WATER II study. | There were no reports of postoperative de novo erectile dysfunction, whereas postoperative de novo ejaculatory dysfunction, defined as losing the ability to emit seminal fluid, was observed in 10.8% of men.<br><br>Clavien-Dindo grade 2 to 4 adverse events were similar across studies. In the only randomised study, the Clavien-Dindo grade 2 to 4 adverse events were similar between water-jet ablation and TURP.<br><br>Men with low baseline ISI scores (4 or less) had modest perioperative rises in ISI score, but values reduced back to baseline with all prostate volumes. In men with clinically significant incontinence (baseline score above 4), ISI scores improved in men with both small and large prostates. |

| First author, date | Efficacy outcomes | Safety outcomes |
|---|---|---|
| | Improvements in IPSS, IPSS QoL, Qmax and PVR were independent of both prostate size and presence or absence of median lobe.<br><br>Improvements in both Qmax and PVR were large and clinically important across all subgroups.<br><br>**Surgical retreatment=0.7%** (95% CI 0.1% to 2.0%) | |
| Gilling, 2020 and 2022 | **Change in IPSS from baseline to 6 months** (primary efficacy endpoint)<br>• Water-jet ablation=16.9 points<br>• TURP=15.1 points,<br>p<0.0001 for non-inferiority, p=0.1346 for superiority<br><br>**Outcomes at 3-year follow up**<br>At 3 years, there were 97 patients in the water-jet ablation group and 55 patients in the TURP group.<br><br>**IPSS reduction, mean (SD)**<br>• Water-jet ablation=14.4 (6.8) points (64% reduction)<br>• TURP=13.9 (8.6) points (61% reduction)<br>p=0.6848 for difference between groups<br>78% of men in the water-jet ablation group and 82% of men in the TURP group had improvements of at least 5 points from baseline. | **Rate of adverse events at 3 months**<br>• Water-jet ablation=26%<br>• TURP=42%,<br>p=0.0149 for superiority<br><br>**Persistent Clavien-Dindo grade 1 events at month 3**<br>• Water-jet ablation=7%<br>• TURP=25%, p=0.0004<br><br>**Rate of grade 2 and above events at month 3**<br>• Water-jet ablation=20%<br>• TURP=23%, p=0.3038<br><br>**Urethral stricture at 3 years**<br>• Water-jet ablation=0.9% (1/116) |

| First author, date | Efficacy outcomes | Safety outcomes |
|---|---|---|
| | For men with larger prostates (50 ml or above), the mean reduction was 3.5 points higher in the water-jet ablation group compared with the TURP group (p=0.0125).<br><br>**Improvement in IPSS QoL score, mean (SD)**<br>• Water-jet ablation=3.2 (1.8) points<br>• TURP=3.2 (1.7) points<br>p=0.7845 for difference between groups<br><br>**Improvements in Qmax, mean (SD)**<br>• Water-jet ablation=11.6 (14) ml/second<br>• TURP=8.2 (8) ml/second, p=0.0848<br><br>**Mean reduction in PSA**<br>• Water-jet ablation=0.9 ng/dl (p=0.0018 compared with baseline)<br>• TURP=1.1 ng/dl (p=0.002 compared with baseline)<br>p=0.5983 for difference between groups<br><br>**Medical failure** (defined as started on alpha blocker or 5-alpha reductase inhibitors after surgery)<br>• Water-jet ablation=9%<br>• TURP=14% | • TURP=6.2% (4/65)<br><br>**Procedure-related anejaculation**<br>• Water-jet ablation=7%<br>• TURP=25%, p=0.0004<br><br>There were no de novo erectile dysfunction events or incontinence events needing a pad in either arm.<br><br>Changes in MSHQ-EjD were close to 0 for all time points up to 5 years in the water-jet ablation group. Average changes were 2.7 points lower (worse) in the TURP group (p=0.0015). |

| First author, date | Efficacy outcomes | Safety outcomes |
|---|---|---|
| | **Outcomes at 5-year follow up**<br>At 5 years, there were 58 patients in the water-jet ablation group and 32 patients in the TURP group.<br><br>**IPSS reduction, mean (SD)**<br>• Water-jet ablation=15.1 (6.6) points<br>• TURP=13.2 (8.2) points,<br>p=0.2764 for difference between groups<br><br>For men with larger prostates (50 ml or more), the IPSS reduction was 3.5 points greater in the water-jet ablation group compared with TURP (p=0.0123).<br><br>**IPSS QoL score** (mean 4.8 at baseline)<br>• Water-jet ablation=1.6<br>• TURP=1.6<br><br>**Improvements in Qmax, mean (SD)**<br>• Water-jet ablation=8.7 (9.1) ml/second (125% improvement)<br>• TURP=6.3 (7.5) ml/second (89% improvement)<br><br>**Additional treatment for BPH**<br>• Water-jet ablation=6.0% (7/116); 5 TURP, 1 laser, 1 medication | |

| First author, date | Efficacy outcomes | Safety outcomes |
|---|---|---|
| | • TURP=12.3% (8/65); 7 medication, 1 TURP<br><br>**Mean reduction in PSA**<br>• Water-jet ablation=1.0 ng/dl (p=0.0658 compared with baseline)<br>• TURP=0.5 ng/dl (p=0.2969 compared with baseline)<br>p=0.465 for difference between groups | |
| Zorn, 2021;<br>Bhojani N, 2023 | **Outcomes at 3 years**<br><br>**IPSS, mean (SD)**<br>• Baseline=23.2 (6.3)<br>• 3 years=6.5 (5.7), p<0.0001<br>3-year IPSS scores were independent of both baseline IPSS and prostate size.<br><br>**IPSS QoL, mean (SD)**<br>• Baseline=4.6 (1.1)<br>• 3 years=1.1 (1.4), p<0.0001<br><br>In patients reporting catheter use in the 45 days before enrolment, IPSS decreased from 26.3 (7.4) at baseline to 3.7 (2.4) at 3-year follow up. No patient using a catheter before surgery had to return to using a catheter postoperatively. | **Adverse events within 6 months**<br>• Blood transfusion (periprocedural)=5.9% (6/101)<br>• Blood transfusion (delayed, within 30 days)=4.0% (4/101)<br>• Fulguration without transfusion=3.0% (3/101)<br>• Bleeding event not needing transfusion or takeback=2.0% (2/101)<br>• Cardiac event=3.0% (3/101)<br>• Cerebrovascular accident=1.0% (1/101)<br>• Dysuria=3.0% (3/101)<br>• Ejaculatory dysfunction=14.9% (15/101)<br>• Meatal stenosis=3.0% (3/101)<br>• Multisystem organ failure=1.0% (1/101) (caused by undiagnosed underlying condition and unrelated to water-jet ablation)<br>• Other (nonurological)=2.0% (2/101) |

| First author, date | Efficacy outcomes | Safety outcomes |
|---|---|---|
| | Improvements in LUTS were described as clinically important.<br><br>**Qmax, mean (SD)**<br>• Baseline=8.7 (3.4) ml/second<br>• 3 years=18.5 (13.8) ml/second, p<0.0001<br><br>**PVR urinary volume, mean (SD)**<br>• Baseline=131 (125) ml<br>• 3 years=51 (63) ml, p value not reported<br><br>**PSA, mean (SD)**<br>• Baseline=7.1 (5.9) g/dl<br>• 3 years=5.0 (6.0) g/dl, p value not reported<br><br>In men not taking 5-alpha-reductase inhibitors before surgery, PSA was decreased substantially at 3 years (p<0.0001).<br><br>**Additional treatment for BPH**<br>At 3-year follow up, 6% of treated patients needed BPH medication and an additional 3% needed surgical retreatment.<br><br>**Outcomes at 5 years** | • Pain=1.0% (1/101)<br>• Skin infection=1.0% (1/101)<br>• Urethral stricture=1.0% (1/101)<br>• Urinary frequency=2.0% (2/101)<br>• Urinary incontinence=5.9% (6/101)<br>• Urinary retention=1.0% (1/101)<br>• Urinary tract infection=6.9% (7/101)<br>• Urinary urgency=2.0% (2/101)<br>**Adverse events at 6 to 12 months**<br>• Bladder stones=3.0% (3/101)<br>• Bleeding event not needing transfusion or takeback=2.0% (2/101)<br>• Ejaculatory dysfunction=1.0% (1/101)<br>• Haematospermia=1.0% (1/101)<br>• Other (nonurological)=5.9% (6/101)<br>• Prostate cancer=1.0% (1/101)<br>• Urinary incontinence=1.0% (1/101)<br>• Urinary retention=1.0% (1/101)<br>• Urinary tract infection=7.9% (8/101)<br>• Urinary urgency=2.0% (2/101)<br>**Adverse events at 1 to 3 years**<br>• Bleeding event not needing transfusion or takeback=5.0% (5/101)<br>• Chronic cystitis=1.0% (1/101) |

| First author, date | Efficacy outcomes | Safety outcomes |
|---|---|---|
| | **IPSS score, mean (SD)**<br>• Baseline=22.6 (6.4)<br>• 5-year follow-up=6.8 (4.6)<br>Change=15.9 (7.7), p<0.001<br><br>5-year IPSS scores were independent of both baseline IPSS and prostate size.<br><br>**IPSS QoL score, mean (SD)**<br>• Baseline=4.6 (1.0)<br>• 5-year follow-up=1.3 (1.3)<br>Change=3.3 (1.6), p<0.001<br><br>There was an immediate improvement after the procedure with the maximum benefit about 90 days later and sustained thereafter.<br><br>**Qmax mean (SD)**<br>• Baseline=8.6 (3.4) ml/second<br>• 5-year follow-up=17.1 (9.8) ml/second<br>Change=9.2 (11.1), p<0.001<br><br>**PVR urinary volume, mean (SD)** | • Ejaculatory dysfunction=2.0% (2/101)<br>• Erectile dysfunction=2.0% (2/101)<br>• Other (nonurological)=4.0% (4/101)<br>• Rising PSA=5.9% (6/101)<br>• Urinary frequency=5.0% (5/101)<br>• Urinary incontinence=1.0% (1/101)<br>• Urinary retention=2.0% (2/101)<br>• Urinary tract infection=5.0% (5/101)<br>• Urinary urgency=3.0% (3/101)<br><br>**Proportion of patients with events at 3 to 4 years follow-up (n=66)**<br>• Erectile dysfunction (not related to procedure)=1.5%<br>• Haematospermia=1.5%<br>• Haematuria=4.5%<br>• LUTS=1.5%<br>• Prostate cancer=1.5%<br>• Prostatitis=1.5%<br>• Rising PSA=1.5%<br>• Urinary retention=1.5%<br>• Urinary tract infection=3.0% |

| First author, date | Efficacy outcomes | Safety outcomes |
|---|---|---|
| | • Baseline=141 (140) ml<br>• 5-year follow-up=64 (64) ml, p<0.001<br><br>During the 5-year follow-up, 6% of patients were offered BPH medications, on average 34 months after the initial procedure. An additional 3% needed surgical retreatment for LUTS on average 25 months after their initial procedure.<br><br>96.3% of patients were free from a secondary BPH intervention at 5 years (Kaplan–Meier analysis).<br><br>There were no surgical retreatments in year 4 or 5.<br><br>A prespecified subgroup analysis using a baseline prostate volume cutoff of 100 ml showed no difference in efficacy outcomes through 5 years. | **Proportion of patients with events at 4 to 5 years follow-up (n=62 [including 2 who withdrew consent at 5 years])**<br><br>• Erectile dysfunction (non-procedure-related)=1.6%<br>• Haematuria=1.6%<br>• LUTS=1.6%<br>• Prostate cancer=1.6%<br>• Rising PSA=3.2%<br>• Urinary tract infection=3.2%<br><br>There were no bladder neck contractures reported in any of the patients seen at the 5-year follow-up visit, and there were no occurrences of urethral stricture or meatal stenosis reported during the 60-month follow-up. |
| Kaplan-Marans, 2021 | No efficacy data were reported. | **Number and severity of adverse events**<br>• Water-jet ablation (102 events)<br>  ○ Mild=10% (10/102)<br>  ○ Moderate=13% (13/102)<br>  ○ Severe=73% (74/102)<br>  ○ Life-threatening or death=5% (5/102) |

| First author, date | Efficacy outcomes | Safety outcomes |
|---|---|---|
| | | • Prostatic urethral lift (132 events)<br>    ○ Mild=31% (41/132)<br>    ○ Moderate=17% (22/132)<br>    ○ Severe=42% (56/132)<br>    ○ Life-threatening or death=10% (13/132)<br>• Transurethral water-vapour therapy (157 events)<br>    ○ Mild=32% (51/157)<br>    ○ Moderate=52% (82/157)<br>    ○ Severe=13% (21/157)<br>    ○ Life-threatening or death=2% (3/157)<br><br>**Notable complications**<br>• Water-jet ablation<br>    ○ Haematuria=37% (38/102)<br>    ○ Blood transfusion=31% (32/102)<br>    ○ Clot evacuation or irrigation=25% (25/102)<br>    ○ Arterial embolisation=1% (1/102)<br>    ○ Laparotomy=2% (2/102)<br>    ○ Rectal perforation=4% (4/102; these were evaluated by the manufacturer and were thought to be because of misuse of the operator) |

| First author, date | Efficacy outcomes | Safety outcomes |
| --- | --- | --- |
| | | ○ Prostatic capsule perforation=2% (2/102)<br>○ Deep vein thrombosis or pulmonary embolism=1% (1/102)<br>• Prostatic urethral lift<br>○ Haematuria=16% (21/132)<br>○ Blood transfusion=16% (21/132)<br>○ Clot evacuation or irrigation=8% (11/132)<br>○ Pelvic or retroperitoneal haematoma=10% (13/132)<br>○ Arterial embolisation=1% (1/132)<br>○ Percutaneous drainage=1% (1/132)<br>○ Laparotomy=2% (3/132)<br>○ Percutaneous nephrostomy=1% (1/132)<br>○ Ureteral stent=2% (3/132)<br>○ Stone removal=2% (2/132)<br>○ Bladder perforation=1% (1/132)<br>○ Orchiectomy=1% (1/132)<br>○ Implant needing to be removed=12% (16/132)<br>○ Implant causing problem with later procedure=7% (9/132)<br>• Transurethral water-vapour therapy |

| First author, date | Efficacy outcomes | Safety outcomes |
| --- | --- | --- |
| | | ○ Haematuria=15% (24/157)<br>○ Blood transfusion=1% (1/157)<br>○ Clot evacuation or irrigation=4% (6/157)<br>○ Hydrocele infection or epididymitis=3% (5/157)<br>○ Bladder perforation=1% (1/157)<br><br>Water-jet device malfunctions included motion error (n=8), handpiece fracture or attachment malfunction (n=8), scope fracture (n=3), low pressure pump error (n=2), revolutions per minute dysfunction error (n=2), and aspiration and irrigation tube detachment from manifold (n=1). |
| Helfand, 2021 | **Mean operative time, minutes**<br>• Very large prostates=64<br>• Large prostates=55<br>• Average size prostates=40, p<0.001<br><br>**Mean IPSS in men with very large prostates**<br>• Baseline=19<br>• Follow up=7, p<0.001 | There were no reports of incontinence, erectile dysfunction, or ejaculatory dysfunction in the group of men with very large prostates.<br><br>There were no periprocedural blood transfusions needed in the group of men with very large prostates.<br><br>2 of the men with very large prostates had low grade prostate cancer documented on submitted pathological tissue. |

| First author, date | Efficacy outcomes | Safety outcomes |
|---|---|---|
| | **Mean Qmax in men with very large prostates**<br>• Baseline=7 ml/second<br>• Follow up=19 ml/second, p<0.001<br><br>Clinical outcomes were similar regardless of prostate volume (p=0.56 for IPSS and 0.74 for Qmax at follow up).<br><br>**Mean decrease in PSA level**<br>• Very large prostates=35%<br>• Large prostates=45%<br>• Average size prostates=32% | |
| Gloger, 2021 | **Mean operative time**<br>• Water-jet ablation=44.8 minutes<br>• HoLEP=80.5 minutes<br>Difference was described as statistically significant, but p value was not reported.<br><br>**Mean length of hospital stay (days)**<br>• Water-jet ablation=3.9<br>• HoLEP=3.4, p=0.001<br><br>**Catheter time (days)**<br>• Water-jet ablation=4.2<br>• HoLEP=3.0, p=0.002 | **Transurethral revision surgery because of bleeding within 6 weeks of procedure**<br>• Water-jet ablation=13.2%<br>• HoLEP=9.8%, p=0.329<br>Most were within the first 10 days after the procedure.<br><br>**Mean perioperative drop in haemoglobin**<br>• Water-jet ablation=1.37 mg/dl<br>• HoLEP=1.22 mg/dl, p=0.353<br><br>**Need for transfusion**<br>• Water-jet ablation=0% (0/167) |

| First author, date | Efficacy outcomes | Safety outcomes |
|---|---|---|
| | | • HoLEP=0.5% (1/215)<br><br>**Bleeding-related rehospitalisation**<br>• Water-jet ablation=3.6% (6/157)<br>• HoLEP=5.6% (12/215), p=0.468<br><br>Subgroup analysis showed no statistically significant differences in haematuria-related complications and need for transfusion according to prostate volume. |
| Elterman, 2021b | Mean time from removing handpiece to inserting the urinary catheter was 19.9 minutes. | **Postoperative bleeding needing transfusion=0.8% (17/2,089; 95% CI 0.5 to 1.3%)**<br>None of these were more than 3 days after the procedure. The average number of units given was 2.<br>24% (4/17) of the transfusions were in patients who were on anticoagulant or antiplatelet therapy.<br>88% of transfusions happened before a surgeon's sixth water-jet ablation procedure.<br><br>**Return to operating theatre for fulguration to address bleeding=0.6% (12/2,089; 95% CI 0.3 to 1.0%)** |

| First author, date | Efficacy outcomes | Safety outcomes |
|---|---|---|
| Elterman, 2020 | No efficacy data were reported. | **Transfusion=3.9% (31/801)**<br>Most were before hospital discharge and none were more than 30 days after the procedure.<br><br>**Transfusion rate in small volume prostates (mean 35 ml, range 20 to 48 ml)**<br>• Standard traction=1.4%<br>• Robust traction=0.8%<br><br>**Transfusion rate in medium volume prostates (mean 62 ml, range 48 to 77 ml)**<br>• Standard traction=2.5%<br>• Robust traction=5.6%<br><br>**Transfusion rate in large volume prostates (mean 104 ml, range 77 to 280 ml)**<br>• Standard traction=1.7%<br>• Robust traction=7.8% |

## Procedure technique

All the studies used the AQUABEAM system (PROCEPT BioRobotics, US) for water-jet ablation. Different techniques were used to achieve haemostasis at the end of the procedure.

## Efficacy

### IPSS

IPSS was reported as an outcome measure in 6 studies. In the systematic review of 7 studies, the raw mean difference in IPSS from baseline at 3 months was -16.5 (95% CI -15.3 to -17.7, $p<0.001$, $I^2=75\%$). From the available data, improvements in IPSS were sustained at 12 months. At 3 months, the IPSS-QoL pooled estimate was 1.29 compared with 4.63 at baseline ($I^2=51\%$, 7 studies; Chen 2023). In the pooled analysis of 4 trials, the mean improvement in IPSS from baseline was 16 points at 1-year follow up and the mean IPSS QoL score improved from 4.7 at baseline to 1.4 at 1 year (Elterman 2021).

In the randomised controlled trial of 181 men (also included in the pooled analysis), the mean reduction in IPSS was 14.4 points (64% reduction) for those who had water-jet ablation (n=97) and 13.9 points (61% reduction) for those who had TURP (n=55) at 3-year follow up (p=0.6848 between groups). The mean IPSS QoL score improved by 3.2 points in both groups (p=0.7845 between groups). At 5 years, the mean reduction was 15.1 points in the water-jet ablation group (n=58) and 13.2 points in the TURP group (n=32; p=0.2764 between groups). For men with larger prostates (50 ml or more) the IPSS reduction was 3.5 points greater in the water-jet ablation group compared with TURP (p=0.0123). The mean IPSS QoL score improved from 4.8 at baseline to 1.6 in both groups (Gilling 2020 and 2022).

In the prospective single-arm trial of 101 men (also included in the pooled analysis), the mean IPSS reduced from 23.2 at baseline to 6.5 at 3-year follow up (p<0.0001) and from 22.6 to 6.8 at 5-year follow up (p<0.001). The mean IPSS QoL score improved from 4.6 at baseline to 1.1 at 3-year follow up (p<0.0001) and 1.3 at 5-year follow up (p<0.001; Zorn 2021 and Bhojani 2023). In the retrospective cohort study of 251 men, the mean IPSS for men with very large prostates reduced from 19 at baseline to 7 at follow up (mean 7 months, p<0.001; Helfand 2021).

**Qmax**

Qmax was reported as an outcome measure in 5 studies. In the pooled analysis of 4 trials, the mean improvement in Qmax from baseline was 9.4 ml/second at 1-year follow up (Elterman 2021).

In the randomised controlled trial of 181 men (also included in the pooled analysis), the mean improvement in Qmax was 11.6 ml/second for those who had water-jet ablation (n=97) and 8.2 ml/second for those who had TURP (n=55) at 3-year follow up (p=0.0848 between groups). At 5 years, the mean improvement was 8.7 ml/second in the water-jet ablation group (n=58; 125% improvement) and 6.3 ml/second in the TURP group (n=32; 89% improvement; Gilling 2020 and 2022).

In the prospective single-arm trial of 101 men (also included in the pooled analysis), the mean Qmax improved from 8.7 ml/second at baseline to 18.5 ml/second at 3-year follow up (p<0.0001) and from 8.6 to 17.1 ml/second at 5-year follow up (p<0.001; Zorn 2021 and Bhojani 2023). In the retrospective cohort study of 251 men, the mean Qmax for men with very large prostates reduced from 7 ml/second at baseline to 19 ml/second at follow up (mean 7 months, p<0.001; Helfand 2021).

**PVR**

PVR was reported as an outcome measure in 3 studies. In the pooled analysis of 4 trials, the mean improvement in PVR from baseline was 62 ml at 1-year follow up. The improvement in PVR was strongly dependent on baseline PVR (Elterman 2021). In the prospective single-arm trial of 101 men (also included in the pooled analysis), the mean PVR had improved to 51 ml at 3-year follow up compared with 131 ml at baseline (p value not reported). At 5-year follow up it was 64 ml compared with 141 ml at baseline (p<0.001; Zorn 2021).

**PSA**

PSA was reported as an outcome measure in 3 studies. In the randomised controlled trial of 181 men, there was a statistically significant mean reduction in PSA level of 0.9 ng/dl for those who had water-jet ablation (n=97; p=0.0018 compared with baseline) and 1.1 ng/dl for those who had TURP (n=55; p=0.002 compared with baseline) at 3-year follow up (p=0.5983 between groups). At 5 years, the mean reduction was 1.0 ng/dl in the water-jet ablation group (n=58; p=0.0658 compared with baseline) and 0.5 ng/dl in the TURP group (n=32; p=0.2969 compared with baseline and p=0.465 between groups; Gilling 2020 and 2022).

**Need for additional treatment**

The need for additional medical or surgical treatment was reported in 4 studies. In the pooled analysis of 4 trials, the rate of surgical retreatment after 1 year was 0.7% (95% CI 0.1% to 2.0%; Elterman 2021). In the randomised controlled trial of 181 men, medical failure (defined as started on alpha blocker or 5-alpha reductase inhibitors after the procedure) was reported for 9% of men who had water-jet ablation and 14% of men who had TURP at 3-year follow up. At 5 years, 6% (7/116) of men who had water-jet ablation group needed additional treatment (5 TURP, 1 laser and 1 medication) compared with 12% (8/65) in the TURP group (7 medication, 1 TURP; Gilling 2020 and 2022). In the prospective single-arm trial of 101 men, 6% of men needed BPH medication and an additional 3% needed surgical retreatment at 3- and 5-year follow up (Zorn 2021 and Bhojani 2023).

## Safety

### Unspecified adverse events

The rate of Clavien-Dindo grade 2 and above events within the first 3 months was similar for water-jet ablation (20%) and TURP (23%) in the randomised controlled trial of 181 men (p=0.3038). The rate of grade 1 events was statistically significantly lower in the water-jet ablation group (7% compared with 25%, p=0.0004; Gilling 2020 and 2022).

In the study by Kaplan-Marans et al. (2021) there were 102 events associated with aquablation, 132 associated with prostatic urethral lift and 157 associated with transurethral water-vapour therapy reported on the FDA MAUDE database during the same time period (2015 to 2020). Of the reported events, there were 79 (78%) described as severe or life-threatening for water-jet ablation, 69 (52%) for prostatic urethral lift and 24 (15%) for transurethral water-vapour therapy.

### Urethral stricture

Urethral stricture was reported as an adverse event in 2 studies. It was reported in 1% (1/116) of men who had water-jet ablation and 6% (4/65) of men who had TURP at 3-year follow up in the randomised controlled trial of 181 men (Gilling 2020 and 2022). Urethral stricture was reported in 1 man within 6 months of the procedure in the single-arm trial of 101 men. In the same study, meatal stenosis was reported in 3% (3/101) of men within 6 months of the procedure (Zorn 2021).

### Rectal perforation

The FDA MAUDE database included 4 reports of rectal perforation. These were evaluated by the manufacturer and were thought to be caused by operator misuse (Kaplan-Marans 2021).

**Bleeding**

Bleeding or the need for blood transfusion was reported as an adverse event in 6 studies, including 3 that were specifically focused on perioperative bleeding.

Reoperation rates for haematuria and other bleeding complications needing return to theatre were reported in 3 studies in the systematic review of 7 studies, ranging from 0% to 8%. Of the 551 men included in the study, 3% returned to the theatre for haemostasis (Chen 2023).

Periprocedural blood transfusion was reported in 6% (6/101) of men and delayed transfusion within 30 days was reported in 4% (4/101) men in the single-arm trial of 101 men. Fulguration without transfusion was reported in 3% (3/101) of men within 6 months. In the same study, a bleeding event that did not need transfusion or return to theatre was reported in 2% (2/101) of men within 6 months, 2% (2/101) of men between 6 and 12 months and 5% (5/101) of men between 12 and 36 months (Zorn 2021).

Transurethral revision surgery because of bleeding within 6 weeks of the procedure was reported in 13% of men who had water-jet ablation and 10% of men who had HoLEP (p=0.329) in the non-randomised comparative study of 382 men (Gloger 2021). Most of these were within the first 10 days of the procedure. In the same study, none of the men who had water-jet ablation and 1 man who had HoLEP needed a transfusion. Bleeding-related readmission to hospital was reported for 4% (6/157) of men who had water-jet ablation and 6% (12/215) of men who had HoLEP (p=0.468).

Postoperative bleeding needing transfusion was reported in 1% (17/2,089) of men in the case series of 2,089 men, all of which were within 3 days of the procedure (Elterman 2021b). Return to theatre for fulguration to address bleeding was reported for 1% (12/2,089) of men. In the case series of 801 men, transfusion was reported in 4% (31/801), most of which were before hospital discharge (Elterman 2020). The risk of transfusion increased as prostate volume increased. Predicted haemoglobin changes were lowest when standard traction was used along with bladder neck cautery.

There were 32 reports of blood transfusion included in the list of notable complications associated with water-jet ablation described in the FDA MAUDE database (Kaplan-Marans 2021).

**Sexual function**

Rates of ejaculatory or erectile dysfunction or change in MSHQ after the procedure were reported in 5 studies.

The overall MSHQ change pooled effect size was -0.6 (95% CI -1.6 to 0.5; p=0.321) before and after intervention at 3 months in the systematic review ($I^2$=74.5%, 4 studies; Chen 2023).

Postoperative de novo ejaculatory dysfunction, defined as losing the ability to emit seminal fluid, was reported in 11% of men in the pooled analysis of 425 men (Elterman 2021). There were no reports of postoperative de novo erectile dysfunction.

Procedure-related anejaculation was reported in 7% of men who had water-jet ablation and 25% of men who had TURP (p=0.0004) in the randomised controlled trial of 181 men. Changes in MSHQ-EjD were close to 0 for all time points up to 5 years in the water-jet ablation group compared with a mean decrease of 2.7 points in the TURP group (p=0.0015). Erectile function, as measured by the IIEF-5, showed no statistically significant changes in either group through 5 years (Gilling 2020 and 2022).

Ejaculatory dysfunction was reported in 15% (15/101) of men within 6 months, 1% (1/101) between 6 and 12 months and 2% (2/101) at 12 to 36 months after the procedure in the single-arm trial of 101 men. Erectile dysfunction was reported in 2 men, both at 12 to 36 months after the procedure (Zorn 2021).

There were no reports of erectile dysfunction or ejaculatory dysfunction in the 34 men with very large prostates included in the cohort study of 251 men (Helfand 2021).

**Urinary incontinence**

Urinary incontinence was reported in 4 studies, 2 of which stated that incontinence scores had improved or that there were no reports of incontinence after the procedure.

In the systematic review of 7 studies, incontinence was reported in 2 studies, with rates of 1% and 5% (Chen 2023).

In the pooled analysis of 425 men it was noted that men with low baseline ISI scores (4 or less) had modest perioperative rises in ISI score, but values reduced back to baseline with all prostate volumes. In men with clinically significant incontinence (baseline score above 4), ISI scores improved (Elterman 2021a). Urinary incontinence was reported in 7% (7/101) of men within 6 months, 1% (1/101) of men at 6 to 12 months and 1% (1/101) of men at 12 to 36 months after the procedure in the single-arm trial of 101 men. Urinary frequency and urinary urgency were reported in 2% (2/101) of men each at 6 months, urinary urgency was reported in 2% (2/101) of men between 6 and 12 months, and urinary frequency was reported in 5% (5/101) of men and urinary urgency was reported in 3% (3/101) of men at 12 to 36 months after the procedure. Dysuria was also reported in 3% (3/101) of men within 6 months of the procedure (Zorn 2021).

There were no reports of incontinence in the 34 men with very large prostates included in the cohort study of 251 men (Helfand 2021).

**Urinary retention**

Urinary retention was reported as an adverse event in 1 study. It was reported in 4% (4/101) of men within 36 months after the procedure in the single-arm trial of 101 men (Zorn 2021).

**Urinary tract infection**

Urinary tract infection was reported as an adverse event in 1 study. It was reported in 7% (7/101) of men within 6 months, 8% (8/101) at 6 to 12 months and 5% (5/101) at 12 to 36 months after the procedure in the single-arm trial of 101 men (Zorn 2021).

**Device malfunction**

Reports of water-jet device malfunctions were described in the FDA MAUDE database review. These included motion error (n=8), handpiece fracture or attachment malfunction (n=8), scope fracture (n=3), low pressure pump error (n=2), revolutions per minute dysfunction error (n=2), and aspiration and irrigation tube detachment from manifold (n=1; Kaplan-Marans 2021).

**Other**

Additional adverse events were reported in the single-arm trial of 101 patients. These included cardiac events (3%), cerebrovascular accident (1%), pain (1%), skin infection (1%), bladder stones (3%), haematospermia (1%) and chronic cystitis (1%; Zorn 2021).

The review of events described on the FDA MAUDE database included the following additional complications: haematuria, clot evacuation or irrigation, arterial embolisation, laparotomy, prostatic capsule perforation and deep vein thrombosis or pulmonary embolism (Kaplan-Marans 2021).

### Anecdotal and theoretical adverse events

Expert advice was sought from consultants who have been nominated or ratified by their professional society or royal college. They were asked if they knew of any other adverse events for this procedure that they had heard about (anecdotal), which were not reported in the literature. They were also asked if they thought there were other adverse events that might possibly occur, even if they had never happened (theoretical).

They described no additional anecdotal adverse events.

They described damage to the bladder neck or sphincter as a theoretical adverse event.

Three professional expert questionnaires for this procedure were submitted. Find full details of what the professional experts said about the procedure in the specialist advice questionnaires for this procedure.

## Validity and generalisability

- The evidence includes data from the UK.
- The evidence includes a randomised, double-blinded controlled trial, comparing water-jet ablation to TURP, with 5-year follow up (Gilling 2020 and 2022).
- The evidence includes a prospective single-arm trial with 5-year follow-up (Zorn 2021 and Bhojani 2023).

- Prostate size varied between studies and the randomised controlled trial only included prostates between 30 ml and 80 ml. Across all studies, prostate volume ranged from 20 ml to 363 ml.
- The study populations included in the systematic review of 7 studies were heterogenous and there was variation in the outcome measures (Chen 2023).
- Some of the evidence was from early use of the technology and the methods used to achieve haemostasis have changed over time.
- The randomised controlled trial included some outcome data to 5 years, which is the longest follow up reported. The authors noted that this was available for a relatively low proportion of men who were enrolled in the study, because the 4 and 5-year follow-up visits coincided with the pandemic caused by COVID-19 (Gilling 2022). The prospective single-arm trial of 101 men reported that 60 (59%) completed 5-year follow up. It noted that about half of those who did not complete the study could be linked to the impact of COVID-19 (Bhojani 2023).
- All 4 studies included in the pooled analysis by Elterman et al. (2021) were sponsored by the device manufacturer. These included the studies by Gilling et al. (2020 and 2022) and Zorn (2021). Authors of the studies by Helfand et al. (2021) and Elterman et al. (2021b) declared a consulting agreement with the device manufacturer, although no funding was provided for the research. Potential conflicts of interest were not reported in the study by Gloger et al. (2021). All authors of the study by Elterman et al. (2020) were investigators for the device manufacturer and data was included from the manufacturer-sponsored trials.
- Ongoing trials:
  - WATER III: A Randomized, Controlled Trial of Aquablation versus Transurethral Laser Enucleation of Large Prostates (80 to 180mL) in Benign Prostatic Hyperplasia (NCT04801381); Germany and UK; n=200; estimated study completion date December 2028.

– Aquablation versus Holmium Laser Enucleation of the Prostate in the Treatment of Benign Prostatic Hyperplasia in Medium to Large Size Prostates: A Prospective Randomized Trial (NCT04560907); Switzerland; n=120; estimated study completion date November 2027.

## Existing assessments of this procedure

The American Urological Association published guidance on the management of lower urinary tract symptoms attributed to benign prostatic hyperplasia in 2021 (Lerner et al. 2021). It includes the following recommendation on transurethral water-jet ablation:

- ‘Robotic waterjet treatment (RWT) may be offered as a treatment option to patients with LUTS/BPH provided prostate volume 30-80cc. (Conditional Recommendation; Evidence Level: Grade C [low certainty]).’

In 2022, the Canadian Urological Association published a guideline on male lower urinary tract symptoms/benign prostatic hyperplasia. It includes the following recommendation on water-jet ablation:

- ‘We suggest that Aquablation be offered to men with LUTS interested in preserving ejaculatory function with prostates <150 cc, with or without a middle lobe (conditional recommendation, evidence level C).’

## Related NICE guidance

### Interventional procedures

- NICE’s interventional procedures guidance on prostatic urethral temporary implant insertion for lower urinary tract symptoms caused by benign prostatic hyperplasia (Recommendation: special arrangements).

- NICE's interventional procedures guidance on transurethral water vapour ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia (Recommendation: standard arrangements).
- NICE's interventional procedures guidance on prostate artery embolisation for lower urinary tract symptoms caused by benign prostatic hyperplasia (Recommendation: standard arrangements).
- NICE's interventional procedures guidance on insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia (Recommendation: normal [standard] arrangements).
- NICE's interventional procedures guidance on laparoscopic prostatectomy for benign prostatic obstruction (Recommendation: special arrangements).
- NICE's interventional procedures guidance on holmium laser prostatectomy (Recommendation: normal [standard] arrangements).
- NICE's interventional procedures guidance on transurethral electrovaporisation of the prostate (Recommendation: normal [standard] arrangements).

## Medical technologies

- NICE's medical technologies guidance on GreenLight XPS for treating benign prostatic hyperplasia.
- NICE's medical technologies guidance on UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia.
- NICE's medical technologies guidance on The PLASMA system for transurethral resection and haemostasis of the prostate.
- NICE's medical technologies guidance on Rezum for treating lower urinary tract symptoms secondary to benign prostatic hyperplasia.

## NICE guidelines

- NICE guideline on lower urinary tract symptoms in men: management.

## Professional societies

- British Association of Urological Surgeons (BAUS).

## Company engagement

NICE asked companies who manufacture a device potentially relevant to this procedure for information on it. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

## References

1. Chen DC, Qu L, Webb H et al. (2023) Aquablation in men with benign prostate hyperplasia: A systematic review and meta-analysis. Current Urology 17: 68–76
2. Elterman, Dean; Gilling, Peter; Roehrborn, Claus; et al. (2021a) Meta-analysis with individual data of functional outcomes following Aquablation for lower urinary tract symptoms due to BPH in various prostate anatomies. BMJ Surgery, Interventions, and Health Technologies 3: e000090
3. Gilling P, Barber N, Bidair M et al. (2020) Three-year outcomes after Aquablation therapy compared to TURP: results from a blinded randomized trial. The Canadian Journal of Urology 27: 10072–79
4. Gilling P, Barber N, Bidair M et al. (2022) Five-year outcomes for Aquablation therapy compared to TURP: results from a double-blind, randomized trial in men with LUTS due to BPH. The Canadian Journal of Urology 29: 10960–68
5. Zorn K, Bidair M, Trainer A et al. (2021) Aquablation therapy in large prostates (80–150 cc) for lower urinary tract symptoms due to benign prostatic hyperplasia: WATER II 3-year trial results. BJUI Compass 3: 130-8
6. Bhojani N, Bidair M, Kramolowsky E et al. (2023) Aquablation therapy in large prostates (80-150 ml) for lower urinary tract symptoms due to benign prostatic hyperplasia: final WATER II 5-year clinical trial results. The Journal of Urology 101097ju0000000000003483
7. Kaplan-Marans E, Martinez M, Wood A et al. (2022) Aquablation, prostatic urethral lift, and transurethral water vapor therapy: a comparison of device related adverse events in a national registry. Journal of Endourology 36: DOI: 10.1089/end.2021.0455

8. Helfand BT, Glaser AP, Kasraeian Ali et al. (2021) Men with lower urinary tract symptoms secondary to BPH undergoing Aquablation with very large prostates (> 150 mL). The Canadian Journal of Urology 28: 10884–88

9. Gloger S, Schueller L, Paulics L et al. (2021) Aquablation with subsequent selective bipolar cauterization versus holmium laser enucleation of the prostate (HoLEP) with regard to perioperative bleeding. The Canadian Journal of Urology 28: 10685–90

10. Elterman DS, Foller S, Ubrig B et al. (2021b) Focal bladder neck cautery associated with low rate of post-Aquablation bleeding. The Canadian Journal of Urology 28: 10610–13

9. Elterman D, Bach T, Rijo E et al. (2020) Transfusion rates after 800 Aquablation procedures using various haemostasis methods. BJU International 125: 568–72

10. Lerner LB, McVary K, Barry M et al. (2021) Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA GUIDELINE PART IId Surgical Evaluation and Treatment. The Journal of Urology 206: 818–826

11. Elterman D, Aubé-Peterkin M, Evans H, et al. (2022) UPDATE – Canadian Urological Association guideline: Male lower urinary tract symptoms/benign prostatic hyperplasia. Canadian Urological Association Journal 16: 245–56

## Methods

NICE identified studies and reviews relevant to transurethral water-jet ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia from the medical literature. The following databases were searched between the date they started to 22 May 2023: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following inclusion criteria were applied to the abstracts identified by the literature search.

- Publication type: clinical studies were included with emphasis on identifying good quality studies. Abstracts were excluded if they did not report clinical outcomes. Reviews, editorials, and laboratory or animal studies, were also excluded and so were conference abstracts, because of the difficulty of appraising study methodology, unless they reported specific adverse events that not available in the published literature.
- Patients with LUTS caused by BPH.
- Intervention or test: transurethral water-jet ablation.
- Outcome: articles were retrieved if the abstract contained information relevant to the safety, efficacy, or both.

If selection criteria could not be determined from the abstracts the full paper was retrieved.

Potentially relevant studies not included in the main evidence summary are listed in the section on other relevant studies.

Find out more about how NICE selects the evidence for the committee.

**Table 4 literature search strategy**

| Databases | Date searched | Version/files |
|---|---|---|
| MEDLINE (Ovid) | 22/05/2023 | 1946 to May 19, 2023 |
| MEDLINE In-Process (Ovid) | 22/05/2023 | 1946 to May 19, 2023 |
| MEDLINE Epubs ahead of print (Ovid) | 22/05/2023 | May 19, 2023 |
| EMBASE (Ovid) | 22/05/2023 | 1974 to May 19, 2023 |
| EMBASE Conference (Ovid) | 22/05/2023 | 1974 to May 19, 2023 |
| Cochrane Database of Systematic Reviews – CDSR (Cochrane Library) | 22/05/2023 | Issue 5 of 12, May 2023 |
| Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library) | 22/05/2023 | Issue 5 of 12, May 2023 |
| International HTA database (INAHTA) | 22/05/2023 | - |

Trial sources searched

- Clinicaltrials.gov
- ISRCTN

- WHO International Clinical Trials Registry

Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

**MEDLINE search strategy**

1 Prostatic Hyperplasia/
2 (Prostat* adj4 (hyperplasia* or adenoma* or hypertroph* or obstruct* or enlarge*)).tw.
3 (BPH or BPO).tw.
4 lower urinary tract symptoms/
5 ((Lower urinary tract adj4 symptoms) or LUTS).tw.
6 nocturia/
7 nocturia.tw.
8 prostatism/
9 prostatism.tw.
10 Urinary Bladder Neck Obstruction/
11 (Bladder adj4 obstruct*).tw.
12 or/1-11
13 Ablation Techniques/ and prostate/
14 Water/
15 13 and 14
16 ((water or aqua*) adj4 ablat*).tw.
17 Aquablation.tw.
18 waterjet.tw.
19 (water adj2 jet).tw.
20 or/15-19
21 12 and 20
22 Aquabeam*.tw.
23 21 or 22
24 Animals/ not Humans/
25 23 not 24

# Other relevant studies

Other potentially relevant studies to the IP overview that were not included in the main evidence summary (table 2 and table 3) are listed in table 5 below.

Case reports have been excluded.

**Table 5 additional studies identified**

| Article | Number of patients and follow up | Direction of conclusions | Reason study was not included in main evidence summary |
| --- | --- | --- | --- |
| Assad A, Nguyen DD, Barber N et al. (2022) WATER vs WATER II 3-year update: comparing Aquablation therapy for benign prostatic hyperplasia in 30-80 cc and 80-150 cc prostates. Urology 165: 268–74 | Pooled analysis of 2 trials (WATER and WATER II)<br>n=282 (217 water-jet ablation)<br>Follow up: 36 months | Three-year follow up demonstrates that Aquablation therapy leads to sustained outcomes, few irreversible complications, and low retreatment rates for the treatment of LUTS/BPH independently of prostate volume. | Data from the 2 trials is already included in the key evidence. |
| Bach T, Barber N, Elterman D et al. (2022) Aquablation outcomes in men with LUTS due to BPH following single versus multi-pass treatments. Urology 169: 167−172 | Pooled analysis of 2 trials (WATER and WATER II)<br>n=282 (217 water-jet ablation)<br>Follow up: 36 months | A second pass of the waterjet had benefits in functional outcomes, as measured by IPSS, IPSS QoL, and Qmax in short-and intermediate-term follow up over a period of 36 months, even though the prostate volume was larger in these groups of patients. A second | Study focuses on the effect of multiple passes of the waterjet. Data from the 2 trials is already included in the key evidence. |

| | | | |
|---|---|---|---|
| | | pass was associated with lower 24- and 36-month IPSS and IPSS QoL and a higher Qmax.<br>There was no increased risk of complications associated with a second pass. | |
| Bach T, Gilling P, Hajj A et al. (2020) First multi-center all-comers study for the aquablation procedure. Journal of Clinical Medicine 9: 603 | Prospective single-arm trial (OPEN WATER)<br>n=178<br>Follow up: 1 year | Real-world evidence shows that the Aquablation procedure is a safe and effective treatment for symptomatic benign prostatic hyperplasia. | Study is included in meta-analysis by Elterman et al. (2021) and Chen et al. (2023). |
| Bach T, Giannakis I, Bachmann A et al. (2019) Aquablation of the prostate: single-center results of a non-selected, consecutive patient cohort. World Journal of Urology 37: 1369–75 | Prospective cohort study<br>n=118<br>Follow up: 3 months | There was significant and immediate improvement of functional voiding parameters Qmax and PVR as well as symptomatic improvement of IPSS and QoL. Aquablation seems to be safe and effective with a low perioperative complication profile even in a non-selected group of patients. | Studies with more patients or longer follow up are included. |
| Bhat A, Blachman-Braun R, Shah HN et al. (2021) Are all procedures for benign prostatic hyperplasia created equal? A systematic review on post-procedural PSA dynamics and its correlation with relief of bladder outlet obstruction. World Journal of Urology; 2021 | Systematic review | Various surgical procedures for BPH result in varying PSA nadirs level. Enucleation procedures and simple prostatectomy produce the most | Review focuses on PSA levels. |

| | | | |
|---|---|---|---|
| | | drastic and sustained decrease in PSA. There is possible indirect evidence suggesting that the level of PSA nadir corresponds closely with the degree of post-operative improvement and durability of the procedure. | |
| Bhojani N, Yafi FA, Misrai V et al. (2021) Review of sexual preservation after novel benign prostatic hyperplasia surgical treatment modalities from Food and Drug Administration clinical trials. Sexual Medicine Reviews 9: 169–73 | Review of randomised controlled trials<br>n=457 (116 water-jet ablation)<br>Follow up: 3 years | For prostates less than 80 mm, Aquablation and prostatic urethral lift showed permanent sexual function preservation in both Male Sexual Health Questionnaire Ejaculatory Function domain short form (ejaculatory function) and IIEF-5 (erectile function) at 3 years after treatment. | Water-jet ablation data was taken from the WATER trial, which is already included in the key evidence. |
| Bhojani N, Nguyen DD, Kaufman RP Jr et al. (2019) Comparison of <100 cc prostates and >100 cc prostates undergoing aquablation for benign prostatic hyperplasia. World Journal of Urology 37: 1361–68 | Prospective single-arm trial (WATER II)<br>n=101<br>Follow up: 3 months | Aquablation clinically normalised outcomes in both prostate cohorts. It is safe and effective in patients with large prostate glands (more than 100 ml) with a smoother learning curve. | Subgroup analysis of WATER II trial, comparing outcomes by prostate size. |
| Bhojani N, Bidair M, Zorn KC et al. (2019) Aquablation for benign prostatic hyperplasia in large prostates (80 to 150 ml): 1-Year Results. Urology 129: 1–7 | Prospective single-arm trial (WATER II)<br>n=101 | The Aquablation procedure is demonstrated to be safe and effective in treating men with large prostates (80 | A report with longer term outcomes from the same study is included. |

| | | | |
|---|---|---|---|
| | Follow up: 12 months | to 150 ml) after 1 year of follow up, with an acceptable complication rate and without a significant increase in procedure or resection time compared to smaller sized glands. | |
| Cantiello F, Fimognari D, Damiano R et al. (2021) Mechanical and ablative minimally invasive techniques for male LUTS due to benign prostatic obstruction: a systematic review according to BPH-6 evaluation. Urologia Internationalis 105: 858–68 | Systematic review<br>48 studies in total (18 on transurethral water-jet ablation) | The procedure shows functional results comparable with the gold standard represented by TURP at follow up of 2 years, but with the main advantage of lower adverse events and anejaculation rates. Compared to TURP, it is characterised by a minimal learning curve related to its operator-free execution. | No meta-analysis.<br>The relevant studies cited in the review are included in the main evidence or in the additional studies table. |
| Chughtai B, Thomas D (2018) Pooled Aquablation results for American men with lower urinary tract symptoms due to benign prostatic hyperplasia in large prostates (60-150 cc). Advances in Therapy 35: 832–38 | Pooled analysis of 2 trials (WATER and WATER II)<br>n=107<br>Follow up: 3 months | Men with LUTS secondary to BPH (60 to 150 ml) in a pooled analysis were treated safely and effectively with Aquablation up to 3 months postoperatively. | Reports of longer term outcomes from the same studies are included. |
| Colicchia M, Corsi P, Romagnoli D et al. (2021) The combination of waterjet ablation (Aquabeam) and holmium laser power for treatment of symptomatic benign prostatic hyperplasia: Early functional results. Central | Retrospective cohort study<br>n=53<br>Follow up: 3 months | The combination of Aquabeam and holmium laser energy for haemostasis is a safe, reproducible technique to treat moderate LUTS in | Small study assessing the combination of water-jet ablation and holmium laser energy for haemostasis. |

| | | | |
|---|---|---|---|
| European Journal of Urology 74: 222–28 | | men with BPH while preserving ejaculation in younger and sexually active individuals. The short-term results showed a lower rate of complications and the encouraging functional results attest that this can be a valid surgical approach for the treatment of BPH. | |
| Dahm P, MacDonald R, McKenzie L et al. (2021) Newer minimally invasive treatment modalities to treat lower urinary tract symptoms attributed to benign prostatic hyperplasia. European Urology Open Science 26: 72–82 | Review<br>12 studies (7 trials) | The current best evidence underlying these newer therapies is limited to few trials (PUL and PAE), short-term follow up of 12 months (Aquablation and Rezum), or sham comparison only (Rezum). | Only 1 study on water-jet ablation was included (Gilling et al., 2019). |
| Das AK, Han TM, Uhr A et al. (2020) Benign prostatic hyperplasia: an update on minimally invasive therapy including Aquablation. The Canadian Journal of Urology 27: 2–10 | Review | Aquablation, Rezum and Urolift are minimally invasive surgical treatment options capable of providing rapid, significant, and durable relief of LUTS secondary to BPH. Each technique demonstrates comparable efficacy to TURP with the added advantages of preserving sexual function, decreasing patient morbidity, | No meta-analysis. |

| | | | |
|---|---|---|---|
| | | and limiting healthcare costs. | |
| Desai M, Bidair M, Bhojani N et al. (2020) Aquablation for benign prostatic hyperplasia in large prostates (80-150 cc): 2-year results. The Canadian Journal of Urology 27: 10147-10153 | Prospective single-arm trial (WATER II)<br>n=101<br>Follow up: 2 years | Two-year prospective multicentre follow up demonstrated that the Aquablation procedure is safe and effective in the treatment of men with LUTS caused by BPH and prostates 80 to 150 ml with durable treatment efficacy, acceptable safety profile and a low retreatment rate. | A report with longer term outcomes from the same study is included.<br>Study is included in systematic review by Chen et al. (2023). |
| Desai M, Bidair M, Zorn KC et al. (2019) Aquablation for benign prostatic hyperplasia in large prostates (80-150 mL): 6-month results from the WATER II trial. BJU international 124: 321–28 | Prospective single-arm trial (WATER II)<br>n=101<br>Follow up: 6 months | At 6 months, 22% of the patients had experienced a Clavien-Dindo grade 2, 14% a grade 3 and 5% a grade 4 adverse event. Bleeding complications needing intervention or transfusion were recorded in 8 patients before discharge and in 6 patients after discharge. The mean IPSS improved from 23.2 at baseline to 6.7 at 3 months, meeting the study's primary efficacy endpoint goal (p<0.001). The maximum urinary flow rate increased from 8.7 to 18.8 ml/second (p<0.001) and post-void residual urine volume decreased | A report with longer term outcomes from the same study is included. |

| | | | |
|---|---|---|---|
| | | from 131 at baseline to 47 at 6 months (p<0.0001). At 6 months, PSA reduced from 7.1 ng/ml at baseline to 4.0 ng/ml, a 44% reduction. | |
| Desai M, Bidair M, Bhojani N et al. (2019) WATER II (80-150 mL) procedural outcomes. BJU International 123: 106–112 | Prospective single-arm trial (WATER II)<br>n=101<br>Follow up: 1 month | No patient needed electrocautery for haemostasis at the time of the primary procedure. The Clavien-Dindo grade 2 or higher event rate at 1 month was 30%. Bleeding complications were recorded in 10 patients (10%) during the index procedure hospitalisation before discharge and included 6 (6%) perioperative transfusions. | A report with longer term outcomes from the same study is included. |
| Desai MM, Singh A, Abhishek S et al. (2018) Aquablation therapy for symptomatic benign prostatic hyperplasia: a single-centre experience in 47 patients. BJU International 121: 945–51 | Case series<br>n=47<br>Follow up: 3 months | The mean IPSS decreased from 24.4 at baseline to 5 at 3 months; IPSS QoL score decreased from 4.5 to 0.3 points; peak urinary flow rate increased from 7.1 to 16.5 ml/second and post-void residual urine volume decreased from 119 to 43 ml (all p<0.01). | Studies with more patients or longer follow up are included.<br>Study is included in systematic review by Chen et al. (2023). |
| Dhliwayo B, Mukhtar S (2019) Novel surgical treatments for benign prostatic enlargement. | Review | The studies reviewed have all confirmed proof of sustained and | No meta-analysis. |

| | | | |
|---|---|---|---|
| Journal of Endoluminal Endourology 2: e18-e23 | | effective relief of male LUTS symptoms. Aquablation (AQUABEAM System) has good comparable results to TURP, and further evaluation and studies are awaited to evaluate its efficacy. | |
| El Hajj A, Misrai V, Nasrallah AA et al. (2022) Learning curve in aquablation: an international multicenter study. World Journal of Urology 40: 773–79 | Case series<br>n=175<br>Follow up: 3 months | Aquablation is associated with a quick learning curve for the defined outcomes. It provided effective LUTS relief and low complication rates independent of surgeon experience. Haemoglobin drop and ejaculatory function preservation were the 2 factors influenced by the surgeons' learning curve. | Studies with more patients or longer follow up are included. |
| EUnetHTA OTCA27 Authoring Team. Comparative effectiveness of surgical techniques and devices for the treatment of benign prostatic hyperplasia. Collaborative Assessment. Diemen (The Netherlands): EUnetHTA; 2021. Report No.: OTCA27. Available from: https //www.eunethta.eu. | Systematic review<br>84 randomised controlled trials (1 on water-jet ablation) | Minimally invasive technologies are expected to reduce the short- and long-term side effects of standard surgical treatments for BPH (in particular in comparison to TURP) while preserving the effectiveness for functional outcomes. | The review only includes 1 randomised controlled trial on water-jet ablation, which is already described in the key evidence. |
| Fiori C, Checcucci E, Gilling P et al. (2020) All you need to | Systematic review | The results of this systematic review, | The review only includes |

| | | | |
|---|---|---|---|
| know about "Aquablation" procedure for treatment of benign prostatic obstruction. Minerva urologica e nefrologica = The Italian Journal of Urology and Nephrology 72: 152–61 | 1 randomised controlled trial (WATER)<br>n=184 (117 water-jet ablation) | based on a single RCT that compared Aquablation with TURP in prostates 30-80 ml in size, confirmed that Aquablation has at least a similar efficacy as TURP, but has a better safety profile, allows shorter resection times, and has a lower risk of retrograde ejaculation.<br>Moreover, in some subcategories of patients (for example, when prostate volume is more than 50 ml) functional outcomes of Aquablation are better than those of TURP. | 1 randomised controlled trial, which is already described in the key evidence. |
| Ghiraldi E, Higgins AM, Sterious S (2022) Initial experience performing "Cautery-Free Waterjet Ablation of the Prostate". Journal of Endourology 36: 1237–42 | Case series<br>n=32<br>Follow up: 30 days | Performing waterjet ablation of the prostate without the use of electrocautery after waterjet treatment to control bleeding resulted in significant bleeding complications (25% of our cohort) during our initial experience. A combination of traction and focal bladder neck electrocautery is the best strategy to minimise bleeding complications after Aquablation. | Studies with more patients or longer follow up are included. |

| | | | |
|---|---|---|---|
| Gilling P, Barber N, Bidair M et al. (2019) Two-year outcomes after Aquablation compared to TURP: efficacy and ejaculatory improvements sustained. Advances in Therapy 36: 1326–36 | Randomised controlled trial (WATER)<br>n=181<br>Follow up: 2 years | Two-year efficacy outcomes after TURP and Aquablation were similar, and the rate of surgical retreatment was low and similar to TURP. | A more recent report with longer term outcomes is included. |
| Gilling PJ, Barber N, Bidair M et al. (2019) Randomized controlled trial of Aquablation versus transurethral resection of the prostate in benign prostatic hyperplasia: one-year outcomes. Urology 125: 169–73 | Randomised controlled trial (WATER)<br>n=181<br>Follow up: 1 year | The 1-year outcomes after TURP and Aquablation were similar and the rate of late procedure-related complications was low. | A more recent report with longer term outcomes is included. |
| Gilling P, Barber N, Bidair M et al. (2018) WATER: A double-blind, randomized, controlled trial of Aquablation R vs transurethral resection of the prostate in benign prostatic hyperplasia.<br>The Journal of Urology 199: 1252–61 | Randomised controlled trial (WATER)<br>n=181<br>Follow up: 6 months | Surgical prostate resection using Aquablation showed noninferior symptom relief compared to transurethral prostate resection but with a lower risk of sexual dysfunction. Larger prostates (50 to 80 ml) demonstrated a more pronounced superior safety and efficacy benefit. | A more recent report with longer term outcomes is included. |
| Gilling P, Anderson P, Tan A (2017) Aquablation of the prostate for symptomatic benign prostatic hyperplasia: 1-year results. The Journal of Urology 197: 1565–72 | Prospective single-arm trial<br>n=21<br>Follow up: 1 year | Mean IPSS score improved from 23.0 at baseline to 6.8 at 12 months ($p<0.0001$) and Qmax increased from 8.7 to 18.3 ml per second ($p<0.0001$). There were no important perioperative adverse events. No urinary incontinence | Studies with more patients or longer follow up are included. |

| | | | |
|---|---|---|---|
| | | developed and sexual function was preserved postoperatively. | |
| Gilling P, Reuther R, Kahokehr A et al. (2016) Aquablation – image-guided robot-assisted waterjet ablation of the prostate: initial clinical experience. BJU International 117: 923–29 | Prospective single-arm trial<br>n=15<br>Follow up: 6 months | These preliminary results from this initial study show aquablation of the prostate is technically feasible with a safety profile comparable to other BPH technologies. | Studies with more patients or longer follow up are included. |
| Gross AJ, Becker B, Vogt K et al. (2021) Rectal perforation after aquablation of the prostate: lessons learned the hard way. World Journal of Urology 39: 3441–46 | Case reports<br>n=2 | **Rectal perforation**<br>These 2 cases of a rectal perforation after aquablation of the prostate demonstrate an unusual complication and its complex management. Diagnostic delay complicates its treatment. Therefore, immediate rectoscopy should be done routinely after the procedure. | Case reports of a safety outcome that is already described in the key evidence. |
| Hwang EC, Jung JH, Borofsky M et al. (2019) Aquablation of the prostate for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia. The Cochrane Database of Systematic Reviews 2: cd013143 | Systematic review<br>n=184<br>(1 study)<br>Follow up: 12 months | Based on short-term (up to 12 months) follow up, the effect of Aquablation on urological symptoms is probably similar to that of TURP (moderate-certainty evidence). The effect on quality of life may also be similar (low-certainty evidence). Longer-term data | Review only includes 1 study, which is already described in the key evidence. |

| | | | |
|---|---|---|---|
| | | and comparisons with other modalities appear critical to a more thorough assessment of the role of Aquablation for the treatment of LUTS in men with BPH. | |
| Kasivisvanathan V, Hussain M (2018) Aquablation versus transurethral resection of the prostate: 1 year United States - cohort outcomes. The Canadian Journal of Urology 25: 9317–22 | Randomised controlled trial (WATER)<br>n=90<br>Follow up: 1 year | Surgical prostate resection using Aquablation showed improvement in lower urinary tract symptoms at 1 year comparable to TURP, but with a lower risk of adverse events and ejaculatory dysfunction. | The study presents data from the US cohort of the WATER study. Data from the whole study population is already included. |
| Kasraeian A, Alcantara M, Alcantara KM et al. (2020) Aquablation for BPH. The Canadian Journal of Urology 27: 10378–81 | Case series<br>n=55 | In the setting of a community private urology practice, Aquablation therapy was safe and effective for the treatment of men with BPH regardless of prostate shape or prostate size. | Studies with more patients or longer follow up are included.<br>Study is included in systematic review by Chen et al. (2023). |
| Kim J, Polchert M, Chacko B et al. (2021) Do Minimally invasive benign prostatic hyperplasia treatments preserve sexual function? A contemporary review of the literature. Current Urology Reports 22: 56 | Review | Rezum and Aquablation demonstrated preservation of overall ejaculatory function and erectile function at 36-month follow up. Similar outcomes occurred with UroLift after a 60-month follow up. Erectile function was preserved | No meta-analysis. |

| | | | |
|---|---|---|---|
| | | following prostate artery embolization and iTIND up to 12 months. | |
| Labban M, Mansour M, Abdallah N et al. (2021) Aquablation for benign prostatic obstruction: Single center technique evolution and experience. Investigative and Clinical Urology 62: 210–16 | Case series<br>n=59<br>Follow up: 3 months | At 3 months, the average drop in serum prostate-specific antigen was 37% (p<0.0001) and functional outcomes were considerably improved. There were 14 adverse events in 13 patients (overall rate of 22%), with grade 1 and grade 2 complications comprising 71% of all adverse events. | Studies with more patients or longer follow up are included. |
| Misrai V, Rijo E, Zorn KC et al. (2019) 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. European Urology 76: 667–75 | Case series<br>n=30<br>Follow up: 1 year | The IPSS score improved to 3 at 6 months, with a mean change of 15.6 points (95% CI 13 to 18.2). IPSS improvements persisted at month 12. Qmax improved to 20.4 ml/second at 12 months. The 6-month rates of Clavien-Dindo grade 2 and 3 events were 13%. There were no reports of incontinence or de novo erectile dysfunction. Postoperative de novo ejaculatory dysfunction was observed in 27% of patients. | Studies with more patients or longer follow up are included.<br>Study is included in systematic review by Chen et al. (2023). |

| | | | |
|---|---|---|---|
| Nguyen, DD, Li T, Ferreira R et al. (2023) Ablative minimally invasive surgical therapies for benign prostatic hyperplasia: A review of Aquablation, Rezum, and transperineal laser prostate ablation. Prostate Cancer and Prostatic Diseases https://doi.org/10.1038/s41391-023-00669-z | Review | Aquablation is a surgeon-guided, robot-executed, heat-free ablative waterjet procedure with sustained functional outcomes at 5 years while having no effect on sexual activity. | No meta-analysis. |
| Nguyen DD, Barber N, Bidair M et al. (2021) WATER versus WATER II 2-year update: comparing Aquablation therapy for benign prostatic hyperplasia in 30-80-cm$^3$ and 80-150-cm$^3$ prostates. European Urology Open Science 25: 21–8 | Comparison of results from a randomised controlled trial (WATER) and single-arm trial (WATER II)<br>n=218<br>Follow up: 2 years | Aquablation therapy clinically normalises outcomes among patients regardless of prostate size or shape. The advantages, namely short operative times and smooth learning curves for clinical outcomes, are comparable for both small-to-moderately-sized and large prostates. These findings suggest that the effectiveness of Aquablation is independent of prostate size and that outcomes are durable for up to 2 years of follow up. | Data from the 2 trials is already included in the key evidence. |
| Nguyen DD, Mantri SS, Zorn KC et al. (2021) 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. Urology 153: 250–55 | Case-control study<br>n=51 | 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 | Small study, focusing on technique. |

| | | | |
|---|---|---|---|
| | | ejaculatory function after Aquablation. | |
| Nguyen DD, Barber N, Bidair M et al. (2020) 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 International 125: 112–22 | Comparison of results from a randomised controlled trial (WATER) and single-arm trial (WATER II)<br>n=217<br>Follow up: 12 months | Water-jet ablation clinically normalises outcomes between patients with 30 to 80 ml prostates and patients with 80 to 150 ml prostates treated for LUTS/BPH, with an expected increase in the risk of complications in larger prostates. Long-term outcomes of procedure durability are needed. | Data from the 2 trials is already included in the key evidence. |
| Nguyen DD, Misrai V, Bach T et al. (2020) Operative time comparison of aquablation, greenlight PVP, ThuLEP, GreenLEP, and HoLEP. World Journal of Urology 38: 3227–33 | Analysis of pooled data | In this analysis of pooled data of multi-surgical techniques and technologies, aquablation provided the lowest operative time across all prostate volumes. Greenlight photovaporisation of the prostate had the longest procedure time for prostates larger than 40 ml. | Pooled analysis, focusing on operative time across different techniques. |
| Pimentel MA, Yassaie O, Gilling P (2019) Urodynamic outcomes after Aquablation.<br>Urology 126: 165–70 | Randomised controlled trial (WATER)<br>n=66<br>Follow up: 6 months | Improvements after Aquablation in objective measures of bladder outlet obstruction were similar to those observed after TURP. | Subgroup analysis of WATER trial, focusing on urodynamic outcomes. |
| Plante M, Gilling P, Barber N et al. (2019) Symptom relief and anejaculation after aquablation or transurethral resection of the prostate: | Randomised controlled trial (WATER)<br>n=181 | In men with moderate-to-severe lower urinary tract symptoms attributable to BPH | Subgroup analysis of WATER trial. |

| | | | |
|---|---|---|---|
| subgroup analysis from a blinded randomized trial. BJU International 123: 651–60 | Follow up: 6 months | and larger, more complex prostates, aquablation was associated with both superior symptom score improvements and a superior safety profile, with a significantly lower rate of postoperative anejaculation. | |
| Probst P, Desai M (2022) Expectations facing reality: complication management after Aquablation treatment for lower urinary tract symptoms. European Urology Focus 8: 1733–35 | Review | The technique for cautery haemostasis after Aquablation is critical. Haemostasis is best achieved using a resectoscope with a hot thin loop to first remove the remnant ‘‘fluffy’’ ablated prostate tissue, revealing deeper bleeding vessels at the level of the capsule that need coagulation. This technique, followed by catheter balloon tension applied to the bladder neck and irrigation, has been adopted by nearly all Aquablation surgeons since 2020. | Review of the management of bleeding complications. |
| Raizenne BL, Bouhadana D, Zorn KC et al. (2022) Functional and surgical outcomes of Aquablation in elderly men. World Journal of Urology 40: 2515–20 | Pooled analysis of 2 trials (WATER and WATER II) n=217 | Elderly men (age 65 and over) showed similar reductions in total IPSS (7.68 points versus 7.12 points) and similar increases in Qmax | Data from the 2 trials is already included in the key evidence. |

| | | | |
|---|---|---|---|
| | Follow up: 3 years | (20.6 ml/second versus 19.3 ml/second) compared to younger men. The ejaculatory dysfunction rate was similar for both cohorts (12% versus 10%). Elderly men experienced similar annual retreatment rates compared to young men (2% versus 1%). | |
| Reale G, Cimino S, Bruno G et al. (2019) “Aquabeam R System" for benign prostatic hyperplasia and LUTS: birth of a new era. A systematic review of functional and sexual outcome and adverse events of the technique. International Journal of Impotence Research 31: 392–99 | Systematic review<br>9 studies<br>n=664 | The Aquabeam System for the treatment of LUTS/BPH has proven to be a safe technique that provides functional outcomes comparable to TURP. About sexual outcomes, the most important data is the low rate of retrograde ejaculation. However, other multicentre randomised trials with larger cohorts and longer follow up are still needed. | No meta-analysis.<br>The studies cited in the review are included in the main evidence or in the additional studies table. |
| Roehrborn CG, Teplitsky S, Das AK (2019) Aquablation of the prostate: a review and update. The Canadian Journal of Urology 26: 20–24 | Review | Aquablation is a safe and effective option for treating LUTS secondary to BPH. Aquablation is a new surgical option that shows very promising short term results, in particular, due to its short resection time | No meta-analysis. |

| | | | |
|---|---|---|---|
| | | regardless of gland size and low rate of sexual side effects. This technology still needs further investigation to confirm durability and efficacy over time. | |
| Sadri I, Arezki A, Couture F et al. (2021) Reasons to overthrow TURP: bring on Aquablation. World Journal of Urology 39: 2291–99 | Review | For small-medium prostates (30 to 80 ml), Aquablation's main advantages include better ejaculatory function and similar functional outcomes compared to TURP. For large prostates (80 to 150 ml), Aquablation demonstrates shorter operative time and superior ejaculatory function when compared to simple prostatectomy, HoLEP, and Greenlight photovaporisation of the prostate. | No meta-analysis. |
| Sajan A, Mehta T, Desai P et al. (2021) Minimally invasive treatments for benign prostatic hyperplasia: systematic review and network meta-analysis. Journal of Vascular and Interventional Radiology 33: 359–367 | Systematic review<br>9 studies<br>n=1,032 (117 water-jet ablation) | The functional outcomes for Rezum, Urolift, Aquablation, and PAE demonstrated similar outcomes in urinary function. Although significant differences in outcomes were limited, Aquablation and PAE were the most durable at 12 months. The benefits of Aquablation are | Only 1 RCT was included on transurethral water-jet ablation (Gilling et al., 2018) |

| | | | |
|---|---|---|---|
| | | overshadowed by bleeding complications and the relatively high transfusion rates. | |
| Suarez-Ibarrola R, Bach T, Hein S et al. (2020) Efficacy and safety of aquablation of the prostate for patients with symptomatic benign prostatic enlargement: a systematic review. World Journal of Urology 38: 1147–63 | Systematic review<br>16 studies<br>n=446 | Data from prospective studies demonstrate that aquablation significantly improves symptom scores and bladder outlet obstruction. Moreover, the WATER study reports comparable outcomes to TURP at 2-year follow up with fewer adverse events and significantly lower anejaculation rates favouring aquablation. A longer follow up of enrolled patients is needed to confirm safety and to assess the efficacy of this procedure compared with other well-established treatment options. | No meta-analysis.<br><br>The relevant studies cited in the review are included in the main evidence or in the additional studies table. |
| Tanneru K, Jazayeri S, Behzad A, Muhammad U et al. (2021) An indirect comparison of newer minimally invasive treatments for benign prostatic hyperplasia: a network meta-analysis model. Journal of Endourology 35: 409–16 | Network meta-analysis<br>4 studies | Patients who had Aquablation had greater improvement in IPSS, QoL, Qmax, and PVR compared to patients who had Rezum and UroLift. Patients in the Aquablation group had similar outcomes to patients who had | Only 1 RCT was included on transurethral water-jet ablation (Gilling et al., 2018) |

| | | | |
|---|---|---|---|
| | | TURP in all domains.<br>Patients in the UroLift group performed better in the sexual function domain compared to patients in the TURP group, but not to patients in the Aquablation group. | |
| Te AE, Sze C, Kaplan SA et al. (2023) Surgical treatment for BPH refractory to medication: robotic water jet ablation vs. TURP functional outcomes from two FDA clinical trials. The Canadian Journal of Urology 30: 11408–13 | Post-hoc analysis of data from WATER and WATER II trials<br><br>n=185<br><br>Follow up: 3 years | Robotic water-jet ablation and TURP are effective BPH therapy in patients who truly failed medical therapy, and robotic water-jet ablation demonstrated this in a much broader prostate size range. | Both trials are already included separately in table 2. |
| Tokarski AT, Leong JY, Roehrborn CG et al. (2021) Aquablation of the prostate: a review and update. The Canadian Journal of Urology 28: 17–21 | Review | At up to 3 years of follow up, Aquablation performs favourably when compared to TURP in terms of alleviation of LUTS and preservation of sexual function compared to TURP. Safety profile was similar between Aquablation and TURP. | No meta-analysis. |
| Whiting D, Ng KL, Barber N (2021) Initial single centre experience of Aquablation of the prostate using the AquaBeam system with athermal haemostasis for the treatment of benign prostatic hyperplasia: 1-year outcomes. World Journal of Urology 39: 3019–24 | Case series<br>n=55<br>Follow up: 1 year | The results from a single centre suggest Aquablation using an entirely athermal approach is a safe cavitating procedure resulting in significant LUTS improvement comparable to | Data was collected as part of the OPEN WATER trial, which is included in the meta-analysis by Elterman et al. (2021). |

| | | | |
|---|---|---|---|
| | | standard cavitating procedures with greater preservation of sexual function. | |
| Yafi FA, Tallman CT, Seard ML et al. (2018) Aquablation outcomes for the U.S. cohort of men with LUTS due to BPH in large prostates (80-150 cc). International Journal of Impotence Research 30 209–14 | Prospective single-arm trial<br>n=82<br>Follow up: 3 months | Aquablation is a safe and effective treatment option for men with large prostates (80 to 150 ml) who have LUTS associated with BPH. | Studies with more patients or longer follow up are included.<br>Study is included in systematic review by Chen et al. (2023). |
| Yee CH, Tang SF, Yuen SKK et al. (2022) Technique, outcome and changes in prostate dimensions in patients with urinary retention managed by aquablation. International Urology and Nephrology 54: 1787–92 | Prospective cohort study<br>n=20<br>Follow up: 6 months | Aquablation provided a consistent improvement in symptoms, uroflowmetry and urodynamic parameters in patients with a urethral catheter. The complication profile from the current series showed that while Aquablation is not necessarily a better procedure than TURP, it is a feasible alternative when the equipment is available. | Studies with more patients or longer follow up are included. |
| Zorn KC, Bhojani N, Goldenberg SL et al. (2019) Aquablation among novice users in Canada: A WATER II subpopulation analysis. Canadian Urological Association Journal 13: e113-e118 | Prospective single-arm trial (WATER II)<br>n=19<br>Follow up: 3 months | In this short-term, 3-month analysis of Canadian men, Aquablation appears to provide a strong surgical alternative in patients with LUTS/BPH due to larger prostate volumes, with | The study presents data from the Canadian cohort of the WATER II study. Data from the whole study population is |

| | | | |
|---|---|---|---|
| | | impressive functional outcomes, relatively short operative time and length of hospital stay, and acceptable complication and low transfusion rates. | already included. |