CHAPTER 1

A NOVEL APPROACH IN ENDOSCOPIC PROSTATE SURGERY: THE REZUM SYSTEM

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INTRODUCTION

Benign prostate hyperplasia (BPH) is a common morbidity, which affects elderly men and leads to lower urinary tract symptoms (LUTS) that negatively affect quality of life (QoL). Current treatment options in LUTS include lifestyle modification, pharmacological treatment and surgical approaches. Surgical approaches are in general performed when other options fail to treat LUTS. Recently, numerous novel minimally invasive techniques have been developed for the treatment of BPH/LUTS. One of the most recent techniques is the Rezum system, which uses thermal energy properties of water vapor. In this chapter, BPH and prostate surgery is briefly explained. The Rezum system is discussed in details, including the procedure, patient selection, advantages, disadvantages, complications and review of the results from the current literature.

BENIGN PROSTATE HYPERPLASIA

Benign prostate hyperplasia (BPH) is a common urological disorder characterized by progressive increase of the size of the prostate gland. BPH is the nonmalignant enlargement of the prostate gland resulting from an increase in volume of epithelial and stromal cells in the periurethral region (1). Its incidence increases with aging and it is reported in 40% in men ≥50 yo and 90% in men over 90 years (2). Prostate volume is also associated with age. An average prostate volume is 20 mL at age 50, while this increases to 34 mL at age 80 (3). In the majority of BPH patients, enlargement of the prostate gland leads to bladder outflow obstruction resulting in lower urinary tract symptoms (LUTS). LUTS has significant negative effects in quality of life (QoL) and symptom progression is associated with progressive enlargement of prostate (4-6).

The severity of BPH symptoms are evaluated with the International Prostate Symptoms Score (IPSS) and the quality of life (QoL) index Clinical stages of BPH according to severity are given in Table 1.

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Table 1. Clinical stages of BPH	
Stage I	No significant obstruction and no bothersome symptoms
Stage II	No significant obstruction but has bothersome symptoms
Stage III	Significant obstruction irrespective of symptoms
Stage IV	Complications of clinical BPH such as urinary tract infection, recurrent haematuria, urinary retention and bladder stones

PROSTATE SURGERY

The current approaches for LUTS resulting from bladder outflow obstruction due to BPH include conservative management such as lifestyle modifications and watchful waiting, pharmacotherapy and surgery. Treatment of BPH is usually based on the severity of LUTS and presence or absence of complications. Pharmacotherapy is associated with unsatisfactory outcomes and adverse effects including reduced sexual functioning, postural hypotension and asthenia. Therefore, surgery is the mainstay of this clinical condition. Men with BPH require surgical approach in the case of refractory urinary retention, persistent hematuria, recurrent urinary tract infection and when other therapies fail (While there are numerous surgical options in the treatment of BPH, transurethral resection of the prostate (TURP) is considered as the gold standard. However, TURP has some limitations such as a high complication rate, prolonged length of stay in hospital and the need for retreatment by 1-2% in a year (7, 8). Complications caused by TURP include erectile dysfunction, urinary tract infection (UTI), urinary incontinence, retrograde ejaculation, and urethral stricture (6, 8). In addition, TURP requires the use of general or spinal anesthesia and the mean hospitalization is 2 days with this method. In order to improve these factors several minimally invasive procedures have been developed. Recently, many innovative interventions have been introduced including thermal energy and water vapor, prostatic artery embolization and mechanical expansion with UroLift (9). All of these novel methods target to avoid the complications with TURP with comparable outcomes. The Rezum system, a novel approach in the treatment of BPH is discussed below.

The Rezum system

Patient selection

Patients with moderate-to-severe LUTS are in general eligible for surgical treatment with the Rezum system. The system used in these patients to relieve symptoms, or when medical treatment fails. Although early clinical experience

has shown excellent outcomes in larger prostate glands, early experience of a urologist for treating BPH patients using the Rezum system should be reserved for smaller glands (10).

Assessment of the patients includes a detailed medical history with physical examination, prostate-specific antigen (PSA), urinalysis, transrectal ultrasonography (TRUS), maximum urinary flow rate (Qmax) and postvoid residual (PVR) urine-volume measurements. In addition, the International Prostate Symptom Score (IPSS) questionnaire is applied. Accordingly, men aged ≥50 years with moderate-to-severe BPH/LUTS, a prostate volume between 20-120 cm3 and an IPSS score ≥13, Qmax ≤15 mL/s and PVR) urine <250 mL are suitable for surgical treatment with the REZUM system (11).

The Rezum thermal therapy system is performed in an ambulatory or office setting. Anxiety and pain is managed on the preference and discretion of the operator. In some cases, conscious sedation may be required. Most patients receive oral agents only or either conscious sedation or prostate block.

The Rezum thermal water vapor treatment method causes no technical or anatomical challenges for patient selection. Inclusion and exclusion criteria are given in Figure 1.

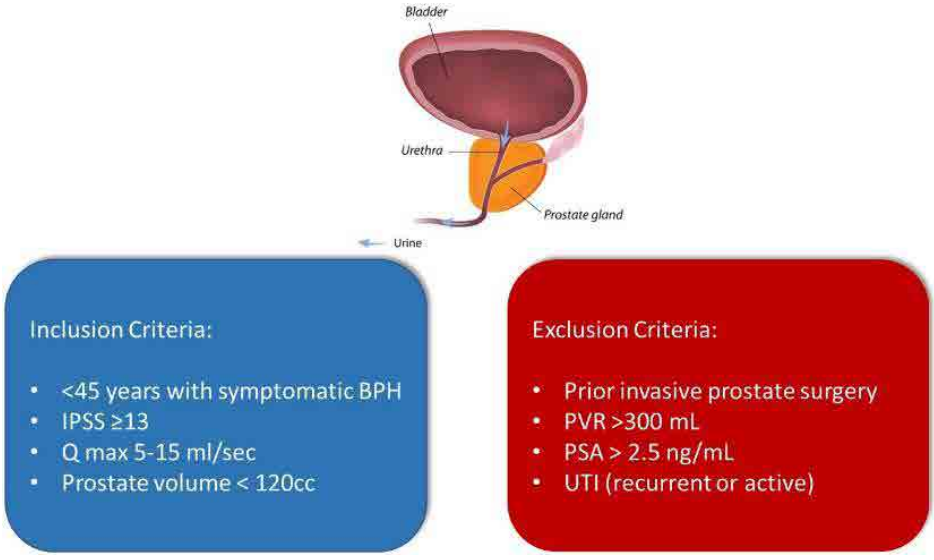

Figure 1. Inclusion and exclusion criteria for the Rezum system. UTI: urinary tract infection.

The procedure

The Rezum system m (NxThera, Inc., Maple Grove, MN) is based on the convective heat transfer that uses thermodynamic features of water (6). Transurethral endoscopic guidance is utilized in water vapor thermal therapy with the Rezum system. The primary goal of the Rezum system is to produce continuous, overlapping lesions parallel to the slope of the prostatic urethra and to eliminate the tissues interfering with the normal functioning (12). Therefore, mapping of the prostate is important. The Rezum system involves a radiofrequency (RF) generator and a single-use delivery tool, which has 4 mm 30°C rod cystoscopy lens. The patient is given a lithotomy position. The treatment device is inserted in the urethra. The bladder and specifically the ureteral orifices are examined. An RD current is applied to an inductive coil. Thermal energy is generated in the form of water vapor. This sterile water vapor is delivered through a polyether ether ketone vapor needle in 9-second injections (7-10 seconds) via 12 small emitter holes in the transurethral device (13). The needle is penetrated to a depth of approximately 10 mm. The water vapor then condenses as a result of contact with body-temperature tissue to create an approximate 12.5 to 2.0 cm lesion. The needle is then withdrawn after each vapor injection and positioned again in 1 cm intervals distally from the previous point to the prostatic tissue (1). The total number of vapor injections in each lobe are based on the length of the prostatic urethra and can be individualized. Each injection delivers nearly 208 calories of thermal energy via conversion of the 0.42 mL sterile water into vapor thermal energy. This liquid state triggers instant cellular necrosis. Cooling of the urethra is provided by saline flush irrigation (14). Both gadolinium-enhanced MRI and post-procedure histological examination have shown that the Rezum system is successful in leading to necrosis in targeted cells, while preserving non-treated tissue (13, 14). Majority of the patients receive sedation only during the procedure.

Advantages

The Rezum system has been adopted widely in the United States of America and Europe. This method is simply to learn compared to other treatment methods such as Holmium laser enucleation of the prostate and TURP. One of the major advantages of the Rezum system is providing rapid and sustainable relief in LUTS and improved quality of life without disrupting sexual functioning in male patients with moderate-to-severe BPH (15). Hypertrophy in all prostatic zones can be treated with this system including both lateral and median zones, prostatic protrusions and elevated central zone in the bladder neck. In a study by Woo et al., patients who underwent the Rezum therapy were followed-up for 36 months

and the patients showed significant improvements in IPSS, QoL, Qmax, and PVR (11). The improvements in urinary flow and LUTS do not impact erectile and ejaculatory functioning of the patients (16). In a study by Gupta et al. it was reported that the Rezum system showed significantly better outcomes in terms of IPSS, QoL and prostate volume (17).

The Rezum system can be performed as a day case procedure in ambulatory or office settings. The average resection time with the Rezum thermal therapy system is approximately 8 minutes. This limits adverse events that may occur and maximize the procedures that will be performed (13). Unlike many other new BPH treatment methods, the Rezum system can treat the prostatic median lobe, increasing the number of patients who are eligible for this procedure (11). The recommended cut-off of 120 cc for prostate volume has been reported so far by conducted studies and it is expected to be expanded in the future.

Disadvantages

In the Rezum system, tissue specimens are not collected to confirm incidental cases of prostate cancers. On the other hand, its exclusion criteria limit the number of patients who are eligible for this procedure. For example, patients with large prostatic burden and those with urinary retention potentially would not be not eligible for the procedure, excluding a considerable portion of BPH patients.

The most important disadvantage of the Rezum system is its novelty and lack of long-term follow-up results of the procedure with RCTs for today (18). In addition, the Rezum system is not suitable for patients with a penile implant or those with artificial urinary sphincter (19). The Rezum system could be theoretically applicable in the treatment of focal nodular growth following TURP procedure, leading to urinary obstruction. However it is yet to be tested and patients with previous interventional procedures have been excluded in previous studies conducted with the Rezum system (20).

Complications

Most postoperative complications of the Rezum system are limited to Clavien–Dindo types I–II. Postoperative complications generally develop due to the acute inflammatory response resulting from ablation of the tissues that lead to irritative LUTS, which may last for 2-3 weeks (19). The most commonly reported complications include urinary retention, hematuria, dysuria, hematospermia, and UTIs (14, 15). These complications usually resolve within a few weeks and no mid-term complication has been reported so far (18).

On the other hand, more serious adverse events have been reported by several studies. In a pilot study by Dixon et al., persistent LUTS symptoms with poor stream, and urinary retention were reported in one patient who was scheduled for TURP procedure at 42 days (14). In a crossover trial by Roehrborn et al., one patient developed urosepsis and one patient suffered with bladder neck contracture and bladder calculi (15). In another randomized controlled study by McVary et al., one patient developed extended urinary retention and one patient was admitted to hospital due to nausea and vomiting after receiving alprazolam (21).

Results from the current literature

The American Urological Association (AUA) recommends the Rezum system for patients with BHP and a prostate volume < 80 g. On the other hand, the European Association of Urology (EAU) guidelines recommend randomized clinical trials against another method to confirm the effectiveness, durability and safety of the Rezum system (22, 23).

In a pilot study conducted by Dixon et al. including 65 patients with BPH, tha patients were followed-up for two years and improvements were achieved in QoL, IPSS, Qmax, PVR and an international index of erectile dysfunction (IIEF) at postoperative first month. The improvement in these parameters was maintained for 24 months, while maximal improvements were obtained at the third month follow-up (14).

In a crossover study by Roehrborn et al. on 53 patients with LUTS and 12-month follow-up duration, similar outcomes were obtained. The Rezum system showed a significant relief of BPH/LUTS symptoms with a non-obstructing uroflow of 16.2±3.8, while erectile function was preserved (15).

In a retrospective study by Darson et al. with 131 patients (mean age: 71 ± 9 years and mean prostate volume: 45±23 gm), the follow-up duration was 12 months. At the end of the follow-up period, IPSS reduced by 45.2%, QoL by 37.8%, PVR by 34.9%, while Qmax improved by 51% compared to the baseline values (14).

In another study by Mollengarden et al. evaluating the experience of a single surgeon's experience with the Rezum system on 129 patients, at the end of 6-month follow-up IPSS reduced by 45.2% and Qmax improved by 71.7% (24).

In a randomized controlled study by McVary et al. evaluating the efficacy of the Rezum system, 4-year follow-up outcomes were published in 2019, including 197 patients from 15 centers. At the end of the follow-up duration, IPSS reduced by 46.7%, QoL by 42.9%, and PVR by 38%. Qmax improved by 42.9% and IIEF by

7.6%. There was no ejaculatory dysfunction reported in this study (12).

In a study by Johnston et al. in 2020, 210 patients who underwent the Rezum procedure were followed-up for one year. In this prospective cohort study, efficacy of the Rezum system was evaluated for the first time in patients with urinary retention. Twenty-five of the 210 patients were catheterized before the procedure and the Rezum system was demonstrated to be effective (25).

In a retrospective study by Bole et al. in 2020, 182 patients underwent the Rezum prostate with 47 of them having a prostate size larger than 80 gm and 59 having urinary retention. The post-operative values were compared between the patients with small-sized and large sized prostates. IPSS was reduced by 45.2% in the patients with small-sized prostates and 39% in the patients with large-sized prostates. Qmax improved by 28.7% in the patients with small-sized prostates and 39.3% in the patients with large-sized prostates. PVR reduced by 47.8% in the patients with small-sized prostates and 51.1% in those with the large-sized prostates (26).

CONCLUSION

The Rezum water vapor based treatment system is considered an effective and safe method in the treatment of LUTS due to BPH with good follow-up outcomes, minor complications, and good patient satisfaction. This system has been shown not to compromise sexual functioning. The Rezum appears an attractive option for patients who want to avoid pharmacotherapy and preserve their sexual function.

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