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BPH-RELATED VOIDING DYSFUNCTION (R LEE, SECTION EDITOR)

Cost-effectiveness of Medical Versus Surgical Therapy for BPH

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Abstract

Purpose of Review Benign prostatic enlargement and obstruction may result in lower urinary tract symptom (LUTS) and have a negative impact on a patient's quality of life. The purpose of this review is to analyze different management options, specifically evaluating the cost-effectiveness of medical versus surgical therapy for BPH.

Recent Findings We performed a detailed review comparing various studies regarding the cost-effectiveness of different management options that were conducted in the last 5 years. When comparing monotherapy with combination therapy in medical treatments, the latter was found to be more cost-effective. Branded combined medical therapies were found to be much more expensive than generic medical therapies but demonstrated the same therapeutic outcome. When looking at operative options, specifically among the transurethral surgeries, there are more invasive options, including mono/bipolar transurethral resection of prostate (TURP) and laser vaporization and there are less invasive modalities (MIST) such as Urolift, Rezūm, transurethral microwave thermotherapy (TUMT), and transurethral needle ablation (TUNA). The findings demonstrated the cost of the more invasive options depended on whether the procedure was conducted as an inpatient or outpatient, with inpatient surgeries being the more expensive. In this context, GreenLight PVP, being performed as an outpatient procedure, was less expensive than TURP. Both of them provided the best relief in BPH symptoms but were found to have a higher incidence of side effects. Accordingly, it has been estimated the cost of MIST to be not only cheaper (except Urolift) than invasive transurethral options, but noted to have fewer side effects, especially in terms of ejaculatory dysfunction.

Summary Although combination generic medical therapy has been shown to be the least costly option, when invasive surgical management, such as TURP or GreenLight PVP as the most expensive, cost by itself is not the only metric to assess a BPH therapy. The more valuable criterion, such as cost-effectiveness, must be examined. In this light, MIST and especially Rezūm do appear to have a cost-effectiveness advantage over the other procedures due to its lower price and fewer side effects, while providing similar clinical efficacy.

Keywords Benign prostatic hyperplasia · Benign prostatic enlargement · BPH · Cost-effectiveness · Cost utility · Comparison BPH treatments

Introduction

Benign prostate enlargement (BPE) is one of the most common urological diseases among the male population. A 2015 US population study estimates that 12.2 million men were actively managed early for BPH-lower urinary tract symptom (LUTS), which accounts for almost 25% of urology visits [1]. In general, the prevalence of BPH increases with age, with more than half of men in their 60s and as many as 90% of men in their 70s and 80s having some LUTS. A recently published meta-analysis of 31 studies demonstrated an increasing prevalence of BPH-LUTS with age, with a pooled prevalence of 14.8%, 20.0%, 29.1%, 36.8%, and 38.4% for age groups of 40–49 years, 50–59 years, 60–69 years, 70–79 years, and 80 years and above, respectively [2]. This number is expected to increase over the next few decades due to a rising life expectancy and increasing numbers of geriatric patients. Consequently, as a result of the aging population, the cost of the treatment to individuals and the health care system is expected to rise proportionally in the future. In this context,

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particularly important to payers is the ability to estimate not just overall cost but cost-effectiveness of the various BPH treatment options. It is hypothesized that prostate enlargement causes lower urinary tract symptoms due to benign overgrowth of the prostatic central zone around the urethra, causing obstruction in the bladder neck and resulting in LUTS. This benign overgrowth, in turn, is caused by increased epithelial and stromal cell proliferation or decreased programmed cell death [1]. Once developed, BPH-LUTS is a chronic condition and, if left untreated, is associated with a progressive development and clinical consequences include urinary tract infection, bleeding, bladder stones formation, acute and chronic urinary retention, overflow incontinence, bladder diverticula, hydronephrosis, and renal failure.

Traditionally, treatment has been focused on alleviating symptoms of the bothersome LUTS and preventing disease complications associated with disease progression. The treatment approaches depend on the patient's overall health status, severity of LUTS, urine flow measurement, presence of disease complications, and prostate size and shape. There are two general treatment categories—conservative and operative management. Conservative management could be further divided into behavioral (e.g., lifestyle changes, fluid restriction, diuretic regimen changes) and pharmacological medication. Operative management consists of traditional surgical approaches, such as simple prostatectomy (open or laparoscopic), endoscopic removal such as transurethral resection of prostate (TURP) or laser vaporization/enucleation, and multiple new modalities, which were merged into one term—minimally invasive surgical therapy (MIST). In most cases with mild to moderate symptoms, a ladder approach to management is preferred, starting with nonpharmacological behavioral modifications, relying on pharmacologic intervention only in the absence of symptom improvement. Surgical treatment is indicated only as a last resort, in the event of failure of pharmacologic therapy, with a preference for traditional endoscopic transurethral resection (TURP). The MIST treatments have taken their place between medical/pharmacological and more invasive surgical approaches as less morbid alternatives.

In this review, we describe and compare the cost and cost-effectiveness of these different types of treatments.

Pharmacological Treatment

There are several types of drugs that are widely used for the treatment of LUTS, including inhibitors of 5-α-reductase (5ARI), selective α-adrenergic receptor blockers (ABs), anticholinergics, β3-adrenoceptor agonists, PDE5 inhibitors, and phytotherapies. While the latter three groups are recommended only in certain clinical scenarios, the ABs and 5ARIs are considered beneficial in most cases and are used as first-line therapy.

While ABs improve symptoms by reducing urinary frequency and increasing urinary flow via relaxation of smooth muscles in the bladder neck and prostatic urethra, 5ARIs slow disease progression and prevent complications by reducing prostate size. Several recent studies estimated the clinical impact and cost-effectiveness of these two groups as monotherapy or in combination (dutasteride or finasteride plus tamsulosin or doxazosin) and demonstrated that combination therapy, especially the fix-dose product Duodart, which contains dutasteride 0.5 mg and tamsulosin 0.4 mg, is more cost-effective than either treatment alone [3]. According to the Medicare website, the annual cost of these medications ranges from $552 to $3588 for monotherapy and from $1656 to $5580 for combination therapy [4•].

In one Canadian study, using a Markov model, it has been estimated, that over a lifetime, the incremental cost-effectiveness ratio of the combination treatment was CAN$25437 per quality-adjusted life year (QALY) gained. At a willingness to pay CAN$50000 per QALY, the probability of combination therapy being cost-effective was 99.6% [3]. Another study published last year shows combination medical treatment costs can vary based on whether the medication is generic or brand, ranging from US$1736 for generic medications which was defined as the cheapest cost among all types of treatment for BPH, to as high as US$7082 for brand combination therapy, which was the most expensive. Despite this high variability in price, the effectiveness and other parameters of the two types of medications were similar [5••]. Despite the proven effectiveness of these medications, many patients remain dissatisfied due to limited improvement of their symptoms or development of medication adverse effects (AEs), such as the variable degree of ejaculatory and orgasmic dysfunction [6]. Whether due to AEs or dissatisfaction with medications, patients often interrupt or discontinue therapy completely. As such, the rate of discontinuation after 12 months of medication therapy ranges from 62 to 91% [7].

Operative Management

In cases where medications have not provided durable improvement and symptom relief, surgical intervention represents a reasonable next step. The American Urological Association recommends certain indications for surgical treatment, including renal insufficiency, refractory retention, urinary tract infections, bladder stones, gross hematuria, and refractory LUTS, or an unwillingness to utilize other therapies (patient preference) [8]. As mentioned earlier, there is a range of surgical options available today in North America, which can be divided into transurethral or transabdominal. The transabdominal approaches, open, laparoscopic, or robotic simple prostatectomy, are considered more invasive and have historically been used in large-sized prostates. Transurethral

approaches may be divided into more invasive, such as mono/bipolar TURP or laser vaporization/enucleation of prostate, and minimally invasive surgical therapies (MIST), such as Urolift (prostatic urethral lift), transurethral microwave therapy (TUMT), water vapor thermal therapy (Rezūm® System), transurethral needle ablation (TUNA). The selection of one or another surgical modality is based on several parameters which include medical background, especially need for continuous anticoagulant medical treatment, prostate size, prostate protrusion into the bladder or presence of large median lobe, bladder stones or diverticula, and, eventually, the skill set of the surgeon.

Monopolar TURP has been the main form of BPH surgical treatment for many years and remains a gold standard for improvements in urinary function to which other therapies are compared. In the last decade, two other modalities, bipolar TURP and laser prostate vaporization (GreenLight PVP) have gained popularity. Both are considered less invasive than monopolar TURP, as well as less morbid. The main difference between monopolar TURP and bipolar TURP is TUR syndrome (dilutional hyponatremia due to prolonged absorption of irrigation fluid), which is unique to monopolar TURP [9]. However, the other possible early- and late-occurring complications are similar across all transurethral interventions and include bleeding, UTI, incontinence, bladder neck stenosis, and urethral stricture [5••] with different probabilities as well as different rates of effectiveness between these treatment options. For example, GreenLight PVP has been proposed as an alternative to TURP in surgically high-risk patients with associated comorbidities, including pacemakers and anticoagulant and anti-platelet medications [10].

In general, the cost of surgical treatment consists of capital and disposible equipment cost, operative time, and hospitalization length. In one US cost analysis published in 2017, TURP was identified as the least costly procedure for BPH management ($1677) if performed as an outpatient surgery. The most costly surgical option was laser prostate vaporization ($6828) performed as an inpatient. Using laser surgery in an outpatient setting reduces the cost to $2127, while the cost of inpatient TURP reaches $4367–$5661. As a result, the study concluded that the inpatient setting increases cost from 1.7 times to 4.9 times [4•].

These data are consistent with several worldwide studies. A retrospective cost-utility analysis performed in Spain on 98 patients demonstrated similar effectiveness of TURP and GreenLight Laser PVP. However, the total cost of GreenLight Laser PVP (£3377) was around £400 less than TURP (£3770), mostly due to shorter hospital admission after GreenLight Laser PVP [11]. Similar results were obtained from an Australian study with decision-analytic model based on a cost-minimization approach. This cost-minimization analysis found no significant difference in direct costs between PVP and TURP, but lower indirect costs associated with GreenLight PVP due to shorter median length of stay (1 vs. 3 days) and as a result lower total cost per procedure ($5791 vs. $6995) [12].

At least three studies in Canada have compared costs associated with GreenLight Laser PVP with those associated with TURP. One study found that GreenLight PVP decreased the total costs by almost $1300 (CAD) per patient. This was explained by the outpatient nature of GreenLight PVP versus TURP, which is usually performed as an inpatient surgery [13]. A more recent Canadian retrospective study compared GreenLight PVP, TURP, and bipolar TURP to determine perioperative hospital costs. This study found more patients were treated on an outpatient basis with GreenLight PVP (93%) versus bipolar TURP (0%) and monopolar TURP (6%). The mean operating room times were 90 min for Greenlight PVP, 78 min for TURP, and 69 min for bipolar TURP. On average, GreenLight PVP costs $1041 (CAD) more than TURP for day surgery cases. However, the total cost of GreenLight PVP was $1127 (CAD) less than monopolar TURP and $1142 (CAD) less than bipolar TURP due to its outpatient nature [14••]. In term of safety, they found lower hospital readmission rates at 30 and 60 days for GreenLight PVP compared with TURP (14% vs. 19%, and 0% vs. 4%, respectively) and lower readmission rates at 30 days compared with bipolar TURP (14% vs. 28%) [14••]. Despite these differences in readmission rates, there was no difference in the quality of life between GreenLight PVP and TURP [13, 15]. A third study by Erman et al. evaluated the cost-effectiveness of TURP or GreenLight PVP as initial treatment for BPH versus standard approach when pharmacotherapy (mono/combination) was used as initial treatment followed by a surgery. In this study, upfront TURP has been shown as the most effective option (15.35 QALYs) followed almost identically by upfront GL-PVP (15.31 QALYs), whereas the upfront alpha-blocker with post GL-PVP was the least effective (15.08 QALYs). Upfront BPH surgeries resulted in QALY gains of 0.12 to 0.27 per person compared with the upfront pharmacotherapy strategies. Probabilistic analysis defined that upfront surgeries provided the highest gain and probability of cost-effectiveness at thresholds over $15,000/QALY. From a cost perspective, upfront surgery strategies were $1221 to $3155 more per person versus an upfront medication treatment with followed operative options. The least expensive (but not most cost-effective) strategy was upfront pharmacotherapy followed by GreenLight PVP ($9807). Upfront TURP was the most expensive option ($12,975), followed by upfront GreenLight PVP ($11,959). The study concluded that treatment approach of using medication as initial treatment followed by TURP for those who fail is less effective and more expensive in comparison with newer modalities and that using delayed GL-PVP instead of TURP for patients that have not shown improvement on initial pharmacotherapy is economically more attractive. Due to the shorter hospitalization and recovery period,

the upfront GL-PVP could be used as preferred surgical modality compared with TURP [16••].

Another recent analysis by Ulchaker and Martinson utilized a Markov model to account for transitions between BPH treatments of cost-effectiveness of most contemporary treatments over 2 years. This study found that invasive surgical options (GreenLight PVP and TURP) have similar cost over 2 years (around $5000) and provided the greatest symptom relief. While their costs are higher than generic combination medical therapy and two MIST modalities (TUNA and Rezūm® System), it is cheaper than branded combination medical therapy and one of the MIST modalities (Urolift). It is important to note, however, that GreenLight PVP–treated and TURP-treated patients have a higher incidence of ejaculatory and orgasmic upset, incontinence, stricture, contracture, or stenosis, and UTI than other MIST modalities. They conclude, that Rezūm is a cost-effective and clinically effective modality in BPH-related LUTS given the observed urinary symptom score improvements over 2 years and minimal transient perioperative side effects. As a result, the authors suggest considering Rezūm as a first-line treatment [5••].

For this reason, many men are still interested in an alternative treatment that must have at least the same effectiveness as drug therapy, but fewer side effects of either drug treatment or traditional surgical options. Minimally invasive surgery therapy (MIST) or office-based BPH procedures, included in the AUA guideline, were listed in this text earlier [8]. While the transurethral microwave therapy (TUMT) and transurethral needle ablation (TUNA) have been studied early and are generally not used in practice anymore, water vapor thermal therapy (Rezūm® System) and Urolift (prostatic urethral lift) are relatively new modalities. All of these options, to different degrees, have shown promising efficacy in the first few years of follow-up. The 5-year prospective study of the prostatic urethral lift was published in 2017 demonstrated durable improvements in quality of life and LUTS relief [17]. A year after, the 3-year outcomes of water vapor thermal therapy experience were presented that also confirmed this modality as another durable alternative for BPH treatment [18]. MIST options have taken the place in BPH treatment for men who have decided not to take medications and wish to avoid possible side effects of sexual and especially ejaculatory dysfunction caused by traditional surgical treatment. However, MIST is not an ideal treatment option for all BPH patients, for example, patients with very large-sized prostates (≥ 80 cm^3) and prostates with a significant intravesical protrusion or extended middle lobe (Urolift only). Nevertheless, these procedures are well tolerated and allow returning to basic activity faster than TURP [4•]. According to Medicare estimates, the cost of Urolift was $2721 per case, whereas water vapor thermal therapy was $1742. However, these estimates are lower than those reported in cost analysis studies [4•]. In the Ulchaker and Martinson analysis, the cost of Urolift was estimated as high as $6346, water vapor thermal therapy at $2582, and TUNA at $2855. All three modalities showed same LUTS relief over 2 years [5••].

Conclusion

BPH is considered a disease detrimental to quality of life, and treatment options must be focused on improving quality of life. In order to reach an optimal patient outcome, the clinician must remain informed of the different treatment options available for BPH management. The existing body of literature, guidelines, and recommendation of different organizations are useful tools in guiding this decision, as well as patient characteristics and the surgeon's familiarity and skill with each of these surgical modalities.

Understanding the cost-effectiveness of these therapeutic modalities is yet another powerful tool that should be included in treatment decision. Combination generic medical therapy has been shown to be the least costly option, with invasive surgical management, such as TURP or GreenLight PVP as the most expensive. Nevertheless, cost by itself is not the only metric to assess a BPH therapy. The more valuable criterion, such as cost-effectiveness, must be examined. The literature suggests that upfront surgical management either GreenLight or TURP is preferable to medical therapy followed by delayed surgical intervention. Additionally, between these two options are several minimally invasive treatments. These modalities, being less invasive and less expensive, provide clinically significant response and have an additional benefit in term of side effects, especially preservation of ejaculatory function. Among the MIST, Rezūm does appear to have a cost-effectiveness advantage over Urolift procedure due to its lower price while providing similar clinical efficacy.

Compliance with Ethical Standards

Conflict of Interest Dr. Dean Elterman declares consultancy and scientific advisory board with Boston Scientific. Dr. Valentin Shabataev and Dr. Ashraf Allahwala declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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