



Photovaporization of the prostate with GreenLight™ Laser 180 W XPS versus transurethral resection of the prostate with monopolar energy for the treatment of benign prostatic enlargement: a cost-utility analysis from a healthcare perspective

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Abstract

Purpose To assess the cost-utility of the photovaporization of the prostate (PVP) with GreenLight™ laser 180 W XPS compared to transurethral resection of the prostate with monopolar energy (M-TURP) for lower urinary tract symptoms (LUTS) due to benign prostatic enlargement (BPE) from a healthcare perspective in Colombia.

Methods We designed a Markov model to compare four health states following treatment with either PVP or M-TURP to estimate expected costs and outcomes. We used the results of the only randomized clinical trial published to date comparing PVP versus M-TURP to estimate surgical outcomes, complications, re-operation and re-intervention rates. Time horizon was defined at 2 years with four cycles of 6 months each. Resource-use estimation involved a random selection of clinical records from a local institution and cost list from public healthcare system. Costs were obtained in Colombian pesos and converted to US dollars. Threshold was defined at three-times the Colombian gross domestic product (GDP) per capita. Quality-adjusted-life-years (QALYs) were used based on the utilities of the available literature. Uncertainty was analyzed with deterministic and probabilistic models using a Monte Carlo simulation.

Results Patients who underwent PVP gained 1.81 QALYs compared to 1.59 with M-TURP. Costs were US\$6797.98 and US\$7777.59 for M-TURP and PVP, respectively. Incremental cost-effectiveness ratio was US\$4452.81 per QALY, favoring PVP as a cost-effective alternative in our context.

Conclusions In Colombia, with current prices, PVP is cost-effective when compared to M-TURP for LUTS due to BPE for a 2-year time horizon.

Keywords PVP · GreenLight laser · TURP · Cost-effectiveness · Cost-utility · QALY

Introduction

The main objective of benign prostatic enlargement (BPE) treatment is to reduce the severity of symptoms, increase urinary flow and prevent possible complications, improving patient's quality of life (QoL) [1]. Several management strategies have been described for this condition, including pharmacological measures and surgical interventions. In the United States, around 40% of patients receive expectant management and 59% medical therapy. Two percent of the patients undergo surgical procedures, where photovaporization of the prostate (PVP) is the most commonly used, followed by TURP [2]. Given the increase of life expectancy

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in the general population and the low adherence to medical therapy in our country [3], a rise in the number of patients requiring intervention for BPE is expected [4].

Open prostatectomy emerged as the standard of treatment during the 20th century and is the definitive treatment for patients with large prostates (> 80 g) associated with severe symptoms. It is the option that carries the greatest symptomatic improvement and is still widely used in Colombia. However, it has the highest rates of complications and associated bleeding [5]. Minimally invasive and endoscopic techniques resulted from the above. Until 2003, the American Urological Association (AUA) considered TURP as the gold standard for treatment of lower urinary tract symptom (LUTS) secondary to BPE, but according to the 2010 AUA guideline, the M-TURP is now considered an option, as it is the use of different laser therapies [6]. The 2017 European Association of Urology (EAU) Male LUTS Guideline states that the 180 W XPS laser should be regarded as the reference for GreenLight™ laser prostatectomy and that the 2-year follow-up data show efficacy and safety outcomes similar to M-TURP, although long-term results are still pending [7].

An advantage of laser technology is its safety profile, which includes less bleeding and fewer complications, especially in patients with high cardiovascular risk, coagulopathies, and patients receiving anticoagulants/antiplatelet drugs [8–10]. Additionally, PVP uses saline solution for irrigation, eliminating the risk of post-TURP syndrome [11, 12]. All of the above results in shorter hospital stay and could lead to lower costs for the healthcare system [13–15].

We aim to assess the cost-utility ratio of PVP with GreenLight™ laser 180 W XPS versus M-TURP in patients with moderate-to-severe LUTS in terms of symptom improvement, peak urinary flow (Q_{\max}) and QoL, as well as QALYs, from a healthcare perspective in Colombia.

Materials and methods

Model development

Following Institutional Ethics Committee approval, an economic de novo evaluation was conducted, assessing cost-utility ratios. We used a Markov model (TreeAge™ Pro Healthcare 2016 software) including four health states: (a) asymptomatic, (b) medical management (c) re-operation (new interventions due to prostatic tissue regrowth) and (d) re-intervention (new interventions due to complications related to M-TURP/PVP).

The perspective of the Colombian healthcare system was assumed following the recommendations of the national methodological reference for economic evaluations endorsed by the Instituto de Evaluación Tecnológica en Salud (IETS) [16].

Patients over 50 years old with moderate-to-severe LUTS (an International Prostate Symptom Score (IPSS) ≥ 10) secondary to BPE were considered, with normal prostate-specific antigen (PSA) and $Q_{\max} \leq 15$, who underwent treatment with the aforementioned surgical techniques.

A 2-year time horizon was defined with four cycles of 6 months each, according to the best evidence available. Outcomes associated with the improvement of symptoms in the patient with BPE, as well as the estimation of QALYs were included.

Markov model

The Markov model is presented in Fig. 1.

Model assumptions

- The cycles were defined every 6 months for 2 years.
- Transition probabilities were adjusted according to the best scientific evidence and opinion of experts.
- The utilities were taken from the literature, assuming that the population characteristics are different from the Colombian population.
- Costs for each state were taken from clinical records based on the frequency and resource use of a high-complexity local hospital.

Cost information

Cost analysis of the interventions implied the identification, measurement and assessment of the cost-generating events according to the alternatives being compared. For this process, we used clinical records from the public healthcare system cost list, a high-complexity local hospital, hospital bills, opinion of experts and the literature review. Direct costs of surgical interventions were included. The unit of measurement corresponds to Colombian pesos (COP) converted to US dollars (USD) according to the official exchange rate (1

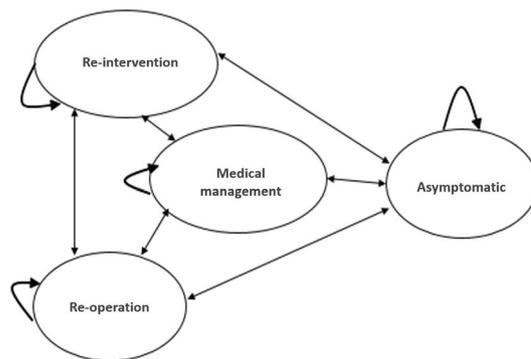


Fig. 1 Markov model for PVP and M-TURP

USD = 2947.85 COP, May 1st 2017). The costs included in the model correspond to each health state (asymptomatic, medical management, re-operation and re-intervention), as well as to each surgical procedure (PVP and M-TURP). A 5% discount rate was used during the 2-year time horizon, using a range of 0–10% in the sensitivity analysis, according to standard of care recommendations.

Effectiveness (outcome measures)

The model’s effectiveness parameters were taken from the literature, specifically from the only multicenter randomized clinical trial published in European Urology by Thomas et al. [17] in 2016, which is known by the urological community as the GOLIATH study and considered by experts as the best available evidence on the subject to date. This study compared PVP with GreenLight™ laser 180 W XPS and M-TURP. It included 29 reference centers in 9 European countries, with a sample consisting of 269 patients with LUTS due to BPE. These patients were randomized to either of these two procedures. In our study, for each surgical intervention, the measurement of treatment outcomes derived from the rate of complications with re-intervention or re-operation requirements according to the Clavien–Dindo classification, and the proportion of patients who required medical management to control their symptoms [18] was validated by a panel of four experts. By the time of the review, no studies with over 2 years of follow-up using the 180 W XPS fiber had been reported in the literature. As an outcome measure for the cost-utility analysis we used QALYs, based on the utilities of the available literature (Table 1).

Sensitivity analysis and uncertainty management

Uncertainty can occur by collecting primary data and/or from assumptions; in turn, it can be controlled by sensitivity analyses. Two types of analyses were performed:

Table 1 Utilities used in the model according to the literature

Health states	Reported utility	Source (Tufts University)
Re-operation	0.86	2013-01-10814
Re-intervention	0.95	2013-01-14843
Medical management or follow-up	0.95	2013-01-14843
Asymptomatic	0.98	2006-01-02810
Urinary incontinence	0.70	2006-01-02810
PVP	0.90	2013-01-14843
M-TURP	0.79	2013-01-10814

PVP photovaporization of the prostate, *M-TURP* transurethral resection of the prostate with monopolar energy

deterministic and probabilistic. A deterministic analysis consists of evaluating the results in a univariate and multivariate manner, considering the ranges defined for each parameter. This analysis is presented with a tornado plot, where the variables that influence incremental results are most appreciated. A probabilistic analysis considers the assignment of ranges and distributions to variables that present uncertainty and is presented by a Monte Carlo simulation, with a hypothetical cohort of patients (1000 iterations). For costs, a triangular distribution was assigned, and for the probabilities and utilities, a beta distribution was used.

Results

Cost-effectiveness of PVP versus M-TURP

In our study, PVP was more cost-effective than M-TURP, gaining 1.81 and 1.59 QALYs, respectively. The cost of the most effective alternative was US\$7777.59, which represents US\$979.62 more than the conventional surgery (US\$6797.98). These results indicate an incremental cost-effectiveness ratio of US\$4452.81 per QALY, suggesting that PVP is a cost-effective alternative with the current willingness-to-pay in Colombia (Fig. 2).

Sensitivity analysis

A tornado plot is presented in Fig. 3. A higher PVP cost can increase the ratio of incremental cost-effectiveness, and a higher cost of surgery with M-TURP could even generate savings for the system. The same graph shows how utilities play an important role in the uncertainty of the model. The deterministic sensitivity analyses by one-way for both cases

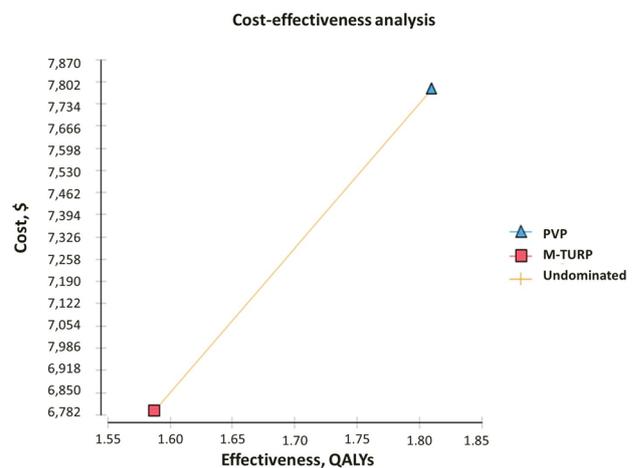
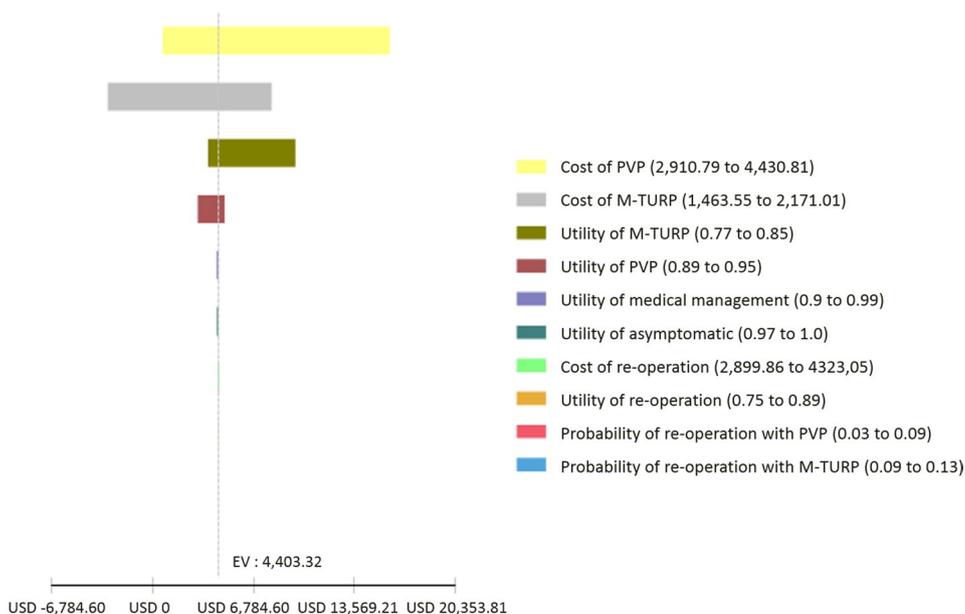


Fig. 2 Results of cost-effectiveness analysis

Fig. 3 Tornado plot



and the two-way multivariate analysis indicated that PVP was more likely to be cost-effective.

In the probabilistic sensitivity analysis, PVP was more expensive but also more effective than M-TURP. All incremental cost-effectiveness results depend on the willingness-to-pay or threshold. In this case, it ranges from US\$0 to US\$43,492.24 per QALY gained. PVP has a high probability of being cost-effective and a greater willingness-to-pay per QALY, which results in a 100% probability of this technology to be cost-effective in the Colombian context.

Monte Carlo simulation

Our results suggest a higher effectiveness and a better relationship for PVP surgery (i.e., PVP is more likely to be cost-effective) than for M-TURP.

Discussion

The incorporation of new technologies always implies the weighing of its advantages versus the cost to be incurred in by the different actors of the healthcare system. We based our study on the results published by Thomas et al. [18] who demonstrated an effectiveness of 83.6% for the management of patients with LUTS using PVP compared to 78.9% with M-TURP. These results were explained not only by the ability of the new technology to remove obstructive prostatic tissue, but also and very importantly, by the reduction of complications found with PVP. The cost of each re-operation and re-intervention also plays a determining role in the cost-effectiveness ratio found in the present analysis. M-TURP is still the most widely used surgical technique in Colombia for

BPE, so we consider this technique as the natural comparator for new technologies.

PVP using GreenLight™ laser 180 W XPS compared to M-TURP is the most effective strategy, but also the most costly option in the Colombian context. According to the willingness-to-pay in Colombia per QALY and controlling the uncertainty of the parameters of the model, in all cases the PVP was cost-effective. However, it is important to highlight the main limitation of our study, which is the lack of reported utilities in the Colombian population. Also, although mid-term effectiveness outcomes for PVP in Colombia are reported in the literature [19], there is a lack of long-term effectiveness parameters for both PVP and M-TURP. Considering utilities and effectiveness parameters are determinant for the estimation of outcomes in terms of cost-effectiveness and QoL, two sensitivity analyses were used to control for the variation of the results, giving us the opportunity to measure this data in our country.

There are few published cost-utility studies on PVP versus M-TURP. Stovsky et al. [13] and later Goh and González [11] conducted a comparative cost analysis of PVP with GreenLight HPS™ 120 W versus M-TURP in two high-complexity private institutions in the US. The study included 470 patients (220 versus 250, respectively) and reported a reduction in the need for hospital stay (11 versus 56, OR 0.18, 95% CI 0.08–0.37) and a shorter hospital stay (1.73 versus 2.59 $p < 0.05$) in the PVP group. Taking into account the average total cost, M-TURP was 19% more expensive than PVP. The authors stated that the highest total cost of M-TURP was most likely influenced by the need and duration of hospital stay, and the rate of complications. Similarly, Bouchier et al. [15] in a randomized clinical trial conducted in Australia reported

a 22% of savings favoring PVP with 80 W fiber, which was attributed to the same variables previously mentioned.

The use of GreenLight™ laser has been cost-effective in other countries such as Spain [20], where the economic evaluation of the use of PVP shows it to be the dominant intervention. Another study conducted in the United Kingdom found that PVP becomes cost saving if over 32% of surgeries for BPE are carried out with this technique [21]. Similar to our results, a study conducted in China found that PVP was more effective but also more expensive, concluding that further analyses are needed to clarify their findings [22].

It is also important to highlight that the safety profile of PVP represents an advantage over M-TURP [8–10]. For example, while the risk of intraoperative transfusion may reach up to 11% in patients receiving M-TURP, with PVP this is null in most series [11].

Additionally, we need to consider the sustainability of implementing this intervention as a recommended clinical practice taking into account a budget-impact analysis according to disease prevalence, technology characteristics, availability and costs in other regions of our country.

The presenting study can significantly influence clinical practice guidelines and impact on savings for the Colombian healthcare system, given the high incidence of BPE and the frequency in which these procedures are performed for its management.

Conclusions

Our results show that, from a healthcare perspective in Colombia, PVP with GreenLight™ laser 180 W XPS for the management of patients 50 years and older with BPE and moderate-to-severe LUTS is a cost-effective strategy with the willingness-to-pay in Colombia over a 2-year time horizon.

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Author contributions JIC: Protocol/project development, data collection or management, manuscript writing/editing. AT: Data collection or management, data analysis, manuscript writing/editing. DR: Protocol/project development, data collection or management, manuscript writing/editing. AB: Data collection or management, manuscript writing/editing. CD: Protocol/project development, data collection or management. CGT: Protocol/project development, manuscript writing/editing. JGC: Protocol/project development, manuscript writing/editing. JCH: Data collection or management, data analysis. DLT: Protocol/project development, data collection or management, data analysis, manuscript writing/editing. MP: Protocol/project development, manuscript writing/editing.

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Compliance with ethical standards

Conflict of interest The authors Juan Ignacio Caicedo, Mauricio Plata and Carlos Gustavo Trujillo declare to have served as instructors of the technique of PVP with GreenLight™ laser 180 W XPS in Colombia through the company Gilmedica and Boston Scientific Corporation. Darío Londoño, Alejandra Taborda, Jonathan Campos, Juan Guillermo Cataño, Cristina Domínguez, Daniela Robledo and Alejandra Bravo declare no conflicts of interest related to the present study.

Ethical approval This study was previously reviewed and approved by our Institutional Ethics Committee.

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